EARLY AND LATE OUTCOMES AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION

Thesis submitted for the degree of

DM Cardiology

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CERTIFICATE

I, **Dr. Ankur Agarwal,** hereby declare that the project in this book, titled **"*EARLY AND LATE OUTCOMES AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION*"** was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

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DECLARATION BY CANDIDATE

I, **Dr Ankur Agarwal** hereby declare that I have done my thesis entitled **"Early and late outcomes after transcatheter aortic valve implantation''** under my allotted guides in the department of Cardiology , SCTIMST.

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CERTIFICATE

We hereby certify that the work in this project titled **"Early and late outcomes after transcatheter aortic valve implantation."** is a certified record of original research work undertaken by Dr Ankur Agarwal in partial fulfilment of requirement for the purpose of award of DM Cardiology under our guidance and supervision.

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Early and late outcomes after transcatheter aortic valve implantation.

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TABLE OF CONTENTS

ABBREVIATIONS

TAVI/TAVR- Trans catheter aortic valve implantation/replacement

MACE- Major adverse cardiac events

Echo- Echocardiogram

ECG- Electrocardiogram

EF- Ejection fraction

TTE- transthoracic Echocardiogram

TEE- Transesophageal echocardiogram

PHV- Prosthetic heart valve

PVL- Paravalvular leak

THV- Transcatheter heart valve

AS- Aortic stenosis

AR- Aortic regurgitation

RV- Right ventricle

Hf- Heart failure

CHF- Congestive heart failure

PAR- Paravalvular aortic regurgitation

TAVT- Transcatheter aortic valve thrombosis

Ppi- Permanent pacemaker implantation

Chb- Complete heart block

Lbbb- Left bundle branch block

Rbbb- Right bundle branch block

SYNOPSIS

Background

Surgical aortic valve replacement has been a widely followed modality for management of severe aortic stenosis. With improving valve designs, TAVI has been now expanded to all strata of surgical risk patients.

Aim

To study the early and late outcomes after transcatheter aortic valve replacement

Methods

This was a retrospective and prospective study which included all patients who underwent TAVI at SCTIMST. Total 23 patients were included in the study, recruited from 2017 to December 2020. 5 patients underwent TAVI in 2020 year, so followup data is obtained upto 1 month, while rest 18 patients had followup data of upto 1 year.

Baseline characteristics including the risk factors, coronary status, valve severity, echo and ecg findings, CT parameters were recorded. Intraprocedural findings including the type of valve, size of valve, need for post dilation, post procedural conduction disturbances, access site complications and stroke were noted. Any complication during the hospital stay was noted. Further followup data upto 1 month and 1 year was obtained which included NYHA class, echo and ecg findings and any complication.

Results

Median STS score was 5.5 +/- 1.88 while median euro score was 7.6+/-5.24. 3 (13%) patients had bicuspid aortic vavle, 3(13%) had TAVI for bioprosthetic avlve, 1(4.3%) had pure aortic regurgitation. 16(69.9%) underwent self expandable valve implantation while rest underwent balloon expandable including Edward sapien and MyVal valve

implantation. Cath study showed median value of peak to peak gradient of 49.2+/-31 while mean gradient of 46.3+/-28 while severe aortic regurgitation was seen in 4(17.4%) patients. Post procedure there was no mortality, 2(8.7%) patients had complete heart block while one had transient complete heart block which recovered. All these patient patients had baseline right bundle branch block at baseline. Stroke was seen in 3(13%) patients while 2(8.7%) had major access site complication which needed surgical intervention.

There was no mortality over the followup period of one year. 83% patients remained in NYHA class 1-2. 2(8.7%) patients had valve leaflet thrombosis while patient prosthesis mismatch was seen in 2(8.7%). Heart failure admissions were seen in 17.3% patients. No patient had more than mild aortic regurgitation on followup. One patient with severe patient prosthesis underwent valve frame fracture, while patients with valve leaflet thrombosis were started on anticoagulation after which gradients improved.

Conclusion

TAVI was found to have good outcomes over a followup period of one year. There was no mortality with significant improvement in functional class of patients. Stroke, heart failure hospitalisations and access site complications were noted to be high.

INTRODUCTION

Severe AS is one of the most common valvular heart disease in elderly and is associated with poor prognosis if left untreated. Surgical valve replacement has been the standard of care in past 50 years but 30-40% patients were deemed unsuitable for surgery due to high risk for procedural risk from multiple comorbidities.[1] For decade, investigators have sought an alternative less invasive approach in these inoperable or high risk patients.

With the first human implantation of transcatheter valve there had been a tremendous shift in valvular management the field of cardiology. The valve designs have been constantly been improving from balloon expandable to self expandable or mechanical expanding Lotus valve. Number of trials have taken place which led to initial approval of TAVR for high risk and inoperable patients but with the constantly improving valve designs, the outcomes have been seen to be comparable with the surgical valve replacement even in intermediate or low risk surgical group.

With the positive results for the TAVI in trileaflet degenerative aortic valve, procedure has been expanding to other groups including bicuspid aortic valve, degenerative bioprosthetic valve, aortic regurgitation. Trials have been going in these groups of patients and with improved valve designs TAVI is likely to be the major intervention replacing the surgical aortic valve replacement.

India with its one of largest population and elderly forming the major constituent of the total aortic stenosis is one of major problem. Due to lack of expertise and high cost of TAVR, it is still not practiced widely in India. Though there has been constant growth in this area every year which also paved way for manufacture of the indigenous Myval valve and Hydra valve in India.

Present study is intended to study the early and late outcomes of all patients who underwent TAVI at our hospital.

REVIEW OF LITERATURE

HISTORY

First percutaneous approach was used for aortic regurgitation management in 1965 where Davis used a parachute configuration cone shaped valve.[2] Subsequently various other designs were used in animal models ,but couldn't be safely implanted in vivo. In 1992 Anderson et al published first report of artificial valve design that could be successfully implanted. It consisted of porcine aortic valve , which was compressed and mounted on a balloon deflation catheter.[3] It was successfully implanted in 9 pig models using midline laparotomy to access abdominal aorta, but device was too large for safe implantation in humans. The first successful valve implantation report in humans was published in 2000 by Bonhoeffer et al.[4] The valve consisted of bovine jugular vein valve sutured onto a platinum/iridium stent and was implanted in a 12 year old boy for pulmonic stenosis and insufficiency. In same year Cribier et al, in affiliation with percutaneous valve technologies Inc.(PVT), introduced percutaneous valve consisting of 3 bovine pericardial leaflets mounted on a balloon expandable stent. One year later in 2001, Paniagua et al., described Paniagua bovine heart valve with smaller crossing profile of 11-16 F which was successfully implanted in animal models. These set the stage for first transcatheter aortic valve implantation by Cribier et al. on April 16, 2002.[5] Patient was a 57 year old man with severe calcific aortic stenosis with medical history of peripheral vascular disease with pervious aorto bifemoral bypass, silicosis, lung cancer in 1999 and chronic pancreatitis. His TTE showed a bicuspid aortic valve with mean gradient of 30 mm Hg , valve area 0.6 cm2, and EF 14%. He underwent initial balloon valvuloplasty with 20 mm balloon after which there was an initial decline in gradients to 13 mm hg but during the ensuing week he went into shock with no improvement on inotropes. As a last resort PVT valve was crimped onto a 30 mm balloon and via 24 F venous access trans-septally valve was deployed at aortic position. Immediately aortic pressure rose and stablized, mean gradient decreased to 6 mm Hg and EF increased to 17%. Though the patient expired 17 weeks after valve implantation due to secondary infection and sepsis. The PVT technology was acquired by Edward Life sciences in 2004. Corevalve company was founded in 2001 by Jacques Seguin and first human Corevalve implantation was done in 2005 by Eberhard Grube.[6] The first retrograde transaortic valve implantation was done by

Paniagua et al in 2005.[7] This revolutionary procedure set the stage for modern management for aortic valve disease.

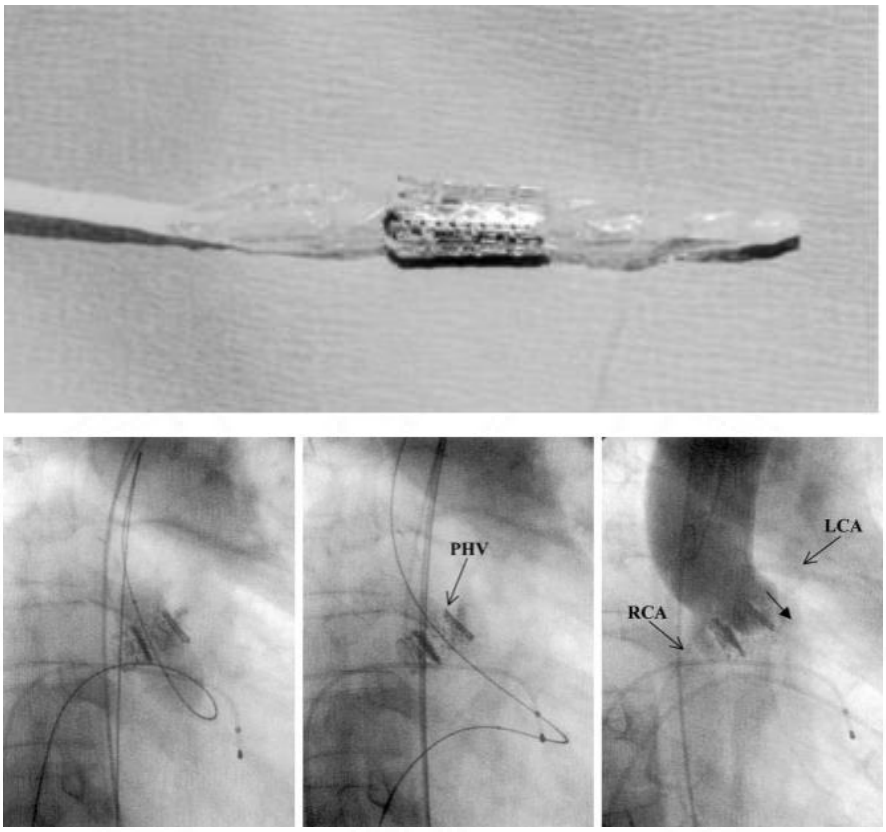

Fig 1- Top- Valve crimped on a 30 mm balloon; Bottom- PHV delivery within the native calcific valve followed by maximal balloon inflation (23 mm).The valve in position at mid part of the native aortic valve, pushing aside the calcific leaflets. Aortic angiogram after PHV implantation showing no aortic regurgitation across the PHV and a mild paravalvular regurgitation

Transcatheter valves

In 2007, Edwards Sapien and Corevalve were the first TAVI products that got CE mark and came to European market and further newer generation valves came upfront. The major type of percutaneous valves used commercially are balloon expandable and self expanding valves.[8]

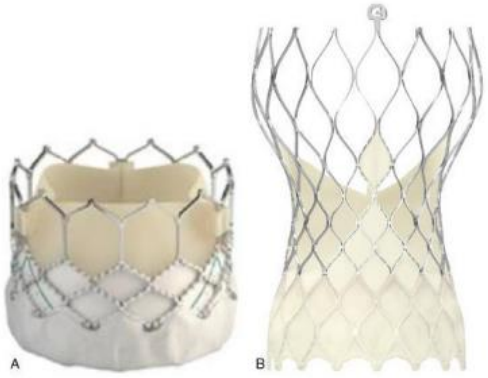

Fig 2- A-Balloon expandable Edward sapien valve B- Self expandable Corevalve

Balloon expandable prostheses include the first-generation Cribier-Edwards valve, the second-generation modified Sapien valve (i.e., Sapien and Sapien XT), and the third-generation Sapien 3 valve (all from Edwards Lifesciences Corp., Irvine, CA). The Edwards Sapien 3 transcatheter valve contains an expandable tubular frame of cobalt-chromium alloy, within which are sewn bovine pericardial leaflets. It has a low delivery profile (14 Fr for 20-, 23-, and 26-mm valves and 16 Fr for the 29-mm valve) and an outer skirt designed to reduce paravalvular leakage (PVLs). For transarterial implantation, the transcatheter valve is crimped onto a Commander delivery catheter (Edwards Lifesciences) and introduced through a sheath placed in the femoral artery. When transfemoral access is not possible, multiple access sites are defined, including subclavian artery, carotid artery, transcaval access using the inferior vena cava to access abdominal aorta, direct aortic access, and transapical access (through the left ventricular [LV] apex. The Sapien 3 valve is balloon expanded within the diseased native valve under rapid ventricular pacing, displacing the diseased native leaflets and anchoring in the calcium of the native aortic annulus. Whereas the Sapien 3 valve is delivered by a 14- or 16-Fr sheath, the older-generation Sapien XT/ NovaFlex transfemoral system used a 16- or 19-Fr sheath. The earliest-generation devices used in the Placement of Aortic Transcatheter Valve (PARTNER) trial required the use of larger-diameter (22– 24 Fr) sheaths.

The self-expanding valve with the longest history and the most published data is the CoreValve system (Medtronic, Minneapolis, MN).[9] The iteration of the CoreValve with the most contemporary data is the Evolut R, a supra-annular valve made from porcine pericardium that features a self-expanding nitinol frame and an extended scalloped sealing skirt that conforms and seals to the native aortic annulus to minimize paravalvular regurgitation. The Evolut-R system can be recaptured to optimize positioning before final valve deployment and does not require rapid ventricular pacing at the time of deployment. The CoreValve Evolut R is compressed within an EnVeo R delivery system catheter (Medtronic) and introduced into the femoral or subclavian artery through a 14-Fr– equivalent system for the 23-, 26-, and 29-mm valves or a 16-Fr– equivalent system for the 34-mm valves. The latest iteration of this valve is the Evolut Pro valve, which has an external pericardial wrap designed to reduce paravalvular regurgitation. This system requires adequate vascular access to allow for a delivery system that is 2-Fr larger than the comparable Evolut R valve.

Indian TAVR valve

Myval THV is indigenously developed at Meril Life Sciences Pvt. Ltd., Vapi, Gujarat, India. Myval THV is characterized by a nickel–cobalt alloy frame composed of a single element – hexagon arranged in a hybrid honeycomb fashion. The trileaflet THV consists of decellularized bovine pericardium tissue, which receives an anticalcification treatment known as AntiCa™ (Meril Life Sciences Pvt. Ltd., Vapi, Gujarat, India) during the manufacturing of Myval THV. The tissue is procured from Australia and fixed with glutaraldehyde at the site. The lower closed cells of Myval THV are covered externally with a sealing cuff, made of polyethylene terephthalate. Myval THV is available in various sizes: traditional (20, 23, 26 and 29 mm), intermediate (21.5, 24.5 and 27.5 mm) and extra-large (30.5 and 32 mm; Myval THV size 32 mm is CDSCO approved and 30.5 mm is pending CDSCO approval and Myval sizes 30.5 and 32 mm are currently not CE marked). The availability of intermediate-size Myval THV broadens the size matrix allowing the heart team to implant a THV without compromising device to annular size ratio. Myval THV is recommended to be crimped on its novel, specially designed, hi-flex, over-the-wire Navigator THV balloon-catheter delivery system. The crimped THV is inserted via specially designed 14 Fr Python sheath.

Other valve systems

The Lotus valve (Boston Scientific, Natick, MA) has a braided nitinol frame with bovine pericardial leaflets that is deployed by controlled mechanical expansion within the annulus. It is fully repositionable before release and has an adaptive seal on the outside of the valve to improve sealing and reduce paravalvular regurgitation. It has been approved for commercial use in patients at high surgical risk and is under active investigation for those at intermediate surgical risk.[10]

The Portico transcatheter aortic heart valve (St. Jude Medical, St. Paul, MN) is a self-expanding, nitinol-based valve that is made of bovine pericardium, delivered transfemorally, and fully repositionable and retrievable. In contrast to the CoreValve leaflets, which are supra-annular, the leaflets with the Portico device are intra-annular.

The Acurate neo valve (Symetis/ Boston, Ecublens, Switzerland) is a transfemoral aortic bioprosthesis composed of a porcine pericardial tissue valve sutured within a

self-expanding nitinol stent. The valve is supra-annular but is designed to have a smaller footprint in the ascending aorta.

The JenaValve (JenaValve Technology, Irvine, CA) is an aortic porcine root valve mounted on a nitinol, self-expanding stent that can be delivered by a transfemoral or transapical approach. The frame design is unique in that it anchors by clipping onto the native leaflets rather than by radial force in the left ventricular outflow tract. It is currently the only transcatheter aortic valve that has been approved for the treatment of AS and AR.

The Edwards Sapien, Medtronic CoreValve, and Boston Scientific Lotus systems are approved for commercial use by the FDA in the United States. The other platforms are commercially available in Europe. Clinical trials are ongoing in the United States for evaluation of the Lotus and Portico valve systems.

Fig 3- A- Acurate neo valve. B- Jena Valve C- Portico valve D- Lotus edge valve

TRIALS

RANDOMISED TAVI TRIALS

PARTNER 1[11-13]

This trial used early generation TAVI valves (i.e., Sapien 23-mm and 26-mm valves with 22-Fr and 24-Fr femoral delivery catheters). Cohort B compared transfemoral TAVR with standard therapy (including BAV). The mean operative mortality risk identified by the Society of Thoracic Surgeons (STS) score was 11.6%. At 1-year follow-up, the rates of death were 50.7% for the standard therapy group and 30.7% for the TAVI group. It was associated with a significant reduction in symptoms at 1 year as assessed by NYHA class. The 5-year follow-up of PARTNER Cohort B

showed that the mortality rate remained lower for the TAVI group compared with that for the standard therapy group (71.8% vs. 93.6%, hazard ratio [HR] = 0.50, 95% confidence interval [CI]: 0.39– 0.65, P < 0.0001). TAVR did not improve the mortality rate with an STS risk score higher than 14.9% on entry into the trial.[14]

COREVALVE U.S. PIVOTAL TRIAL

In the CoreValve U.S. pivotal trial, patients with severe symptomatic AS at high operative risk were randomized to TAVI with the CoreValve or to SAVR. The mean STS score was 7.4%. The death from any cause at 1 year was lower for the TAVR group compared with the surgical group (14.2% vs. 19.1%, P < 0.01 for noninferiority). The major adverse cardiovascular and cerebrovascular events at 1 year were significantly lower for the TAVR group than the surgical group (20.4% vs. 27.3%, P = 0.03).[15]

INTERMEDIATE RISK GROUP TRIALS

PARTNER 2

The PARTNER 2 trial randomized intermediate-risk patients to TAVR with a Sapien XT valve or to SAVR. The mean STS score for each group was 5.8%. The trial showed that TAVR was noninferior to SAVR with respect to the primary end point of death (16.7% after TAVR and 18.0% after surgery, P = 0.001) or disabling stroke (6.2% after TAVR and 6.4% after surgery, P = 0.001) at 2 years. [16]

SURTAVI

The Surgical Replacement and Transcatheter Aortic Valve Implantation (SURTAVI) trial randomized 1746 intermediate-risk patients with severe symptomatic AS to TAVR using of a self-expanding prosthesis or to SAVR. The mean STS score was 4.5%. At 24 months, the estimated incidence of the primary end point of death from any cause or disabling stroke was 12.6% for the TAVR group and 14.0% for the surgery group (95% CI: − 5.2% to 2.3%; posterior probability of noninferiority > 0.999).[17]

TAVR in patients at low surgical risk

PARTNER 3 trial

Patients with severe AS at low surgical risk were randomly assigned to undergo TAVR with balloon-expandable valve or conventional surgery. TAVR was superior to SAVR, with a significantly lower rate of death, stroke, or rehospitalization at 1 year. Similarly, comparing TAVR with a self-expanding valve with SAVR for a composite end point of death or disabling stroke at 24 months, TAVR was found to be noninferior to SAVR.[18]

Notion trial

Patients received the Medtronic CoreValve self-expanding prosthesis. The primary composite outcome of all-cause mortality, MI, stroke for was non inferior for TAVR vs. SAVR at 1 year. At 5 years, rates of death, MI, and stroke were comparable between the two groups[19]

EVOLUTE LOW RISK trial

In low risk patients TAVR with the self-expanding CoreValve Evolut valve was noninferior to SAVR for the primary endpoint of mortality/disabling stroke at 24 months (median STS PROM 1.9%).[20]

MYVAL THV: FIRST-IN-HUMAN (MYVAL-1) STUDY RESULTS AND LANDMARK TRIAL DESIGN

Study included 100 patients with avg. age of 73.6 years with mean STS score of 5.11% (30 centres across India). 30 day outcomes showed excellent clinical and hemodynamic results in term of survival, low stroke rate, lower need for PPI, precise valve position and high procedural success.[21] For validation of results LANDMARK tiral has been designed which will be comparing Myval with the contemporary Edward Sapien and Evolute series.[22]

TAVR REGISTRIES

UK TAVI REGISTRY

The U.K. TAVI registry includes 3980 TAVR procedures performed at 33 centers in UK from 2007 through 2012.[23] Patients received the Sapien/ Sapien XT (Edwards Lifesciences; n = 2036) or the CoreValve (Medtronic; n = 1897) device and a minority

of patients received a Portico (St. Jude; n = 35), Direct Flow (Direct Flow Medical, Santa Rosa, CA; n = 3), or JenaValve (JenaValve; n = 3) device. There was no difference in survival between Sapien and CoreValve devices; however, CoreValve was associated with a higher incidence of post TAVR AR ($P < 0.001$) and need for pacemaker implantation ($P < 0.001$). The rate of pacemaker implantation has decreased with CoreValve, from 29% to 15% in recent years ($P < 0.001$).[24]

US TAVI registry

This registry included 12,182 patients (median age, 84 years; 52% female) undergoing TAVR using the Sapien valve between November 2011 and June 2013 at 299 U.S. hospitals. Median STS score was 7.1%. Rates of death and stroke at 1 year were 23.7% and 4.1%, respectively. The 2017 publication from TVT included 54,782 patients who underwent TAVR through 2015. The data demonstrated a drop in the STS risk score of the patients between 2012 and 2015 (from 7% to 6%; $P < 0.0001$). Outcomes also improved during this time frame, with the in-hospital mortality rate decreasing from 5.7% to 2.9% and 1-year mortality rate decreasing from 25.8% to 21.6%.[25]

TAVI EVOLUTION IN INDIA

In India nearly 2.5–3 lakh patients with AS are likely to be eligible for transcatheter aortic valve replacement (TAVR). The first TAVR in India was done in 2011 in 80-year-old female patient with severe AS with a 26-mm Medtronic CoreValve through the transfemoral route. Currently TAVR is being done in around 30 centres across India, while seven centres are handling the majority of the load.[26]

TAVR valves used in India include both U.S. FDA approved and indigenous valves of which most common valves used are the CoreValve and the Medtronic EvolutR valve. MyVal, the indigenous Indian valve has made a significant impact in the Indian market by virtue of its design, advanced delivery system and lower cost. Another self-expanding valve—Hydra aortic valve (self expanding valve) is slowly gaining popularity in Indian market. Procedure cost for TAVR in India is approximately 35,000 U.S. dollars. The cost of surgical AVR is much less than that of TAVR which makes it the preferred option.[27]

Medical devices are regulated by the Drug Controller General of India (DCGI) within the Central Drugs Standard Control Organization (CDSCO) which is a part of the Ministry of Health and Family Welfare. MyVal got the approval from CDSCO and became the first Indian company to enter the TAVR market.

Asian individuals have a smaller body surface area (BSA), smaller annulus size, smaller dimensions of the sinus of Valsalva and of the sino-tubular junction, low coronary ostia take-off and also smaller iliac and femoral size.[28,29] These differences can cause increased chances of complications and points towards need for smaller devices and better delivery systems. Another anatomic peculiarity among the Indian patients is the high prevalence of BAV which is associated with higher risk of complications compared to trileaflet valve.[30]

PATIENT SELECTION

Before a patient is offered TAVR, surgical risk scores i.e. STS Risk score/Euro Score should be calculated and considered along with NYHA functional class, the preprocedural transvalvular gradient, renal function, vascular surgery or stent, adequacy of transfemoral vascular access, prior stroke, frailty, and pulmonary disease requiring supplemental oxygen. Patients with porcelain aorta are likely to receive greater benefit from TAVR because the procedural risks are lower.[31,32]

Guidelines

Table 1- Valvular heart disease guidelines AHA 2020[33]

Class	LOR	Indication
1	A	1-For symptomatic and asymptomatic patients with severe AS and any indication for AVR who are <65 years of age or have a life expectancy >20 years, SAVR is recommended
1	A	2-For symptomatic patients with severe AS who are 65 to 80 years of age and have no anatomic contraindication to transfemoral TAVI, either SAVR or transfemoral TAVI is recommended after shared decision making about the balance between expected patient longevity and valve durability
1	A	3-For symptomatic patients with severe AS who are >80 years of age or for younger patients with a life expectancy <10 years and no anatomic contraindication to transfemoral TAVI, transfemoral TAVI is recommended in preference to SAVR
1	B	4-In asymptomatic patients with severe AS and an LVEF <50% who are <80 years of age and have no anatomic contraindication to transfemoral TAVI, the decision between TAVI and SAVR should follow the same recommendations as for symptomatic patients
1	B	5-For asymptomatic patients with severe AS and an abnormal exercise test, very severe AS, rapid progression, or an elevated BNP (COR 2a indications for AVR), SAVR is recommended in preference to TAVI
1	A	6-For patients with an indication for AVR for whom a bioprosthetic valve is preferred but valve or vascular anatomy or other factors are not suitable for transfemoral TAVI, SAVR is recommended
1	A	7For symptomatic patients of any age with severe AS and a high or prohibitive surgical risk, TAVI is recommended if predicted post-TAVI survival is >12 months with an acceptable quality of life
1	C	8-For symptomatic patients with severe AS for whom predicted post-TAVI or post-SAVR survival is <12 months or for whom minimal improvement in quality of life is expected, palliative care is recommended after shared decision-making, including discussion of patient preferences and values
2B	C	9-In critically ill patients with severe AS, percutaneous aortic balloon dilation may be considered as a bridge to SAVR or TAVI.

Table 2- Valvular heart disease guidelines ESC 2017[34]

Class	LOR	Indication
1	C	Aortic valve interventions should only be performed in centres with both departments of cardiology and cardiac surgery on site and with structured collaboration between the two, including a Heart Team
1	C	The choice for intervention must be based on careful individual evaluation of technical suitability and weighing of risks and benefits of eachmodality In addition, the local expertise and outcomes data for the given intervention mustbe taken into account
1	B	SAVR is recommended in patients at low surgical risk (STS or EuroSCORE II < 4% or logistic EuroSCORE I < 10%d and no other risk factors not included in these scores, such as frailty, porcelain aorta, sequelae of chest radiation
1	B	TAVI is recommended in patients who are not suitable for SAVR as assessed by the Heart Team
1	B	In patients who are at increased surgical risk (STS or EuroSCORE II >= 4% or logistic EuroSCORE I >= 10% or other risk factors not included in these scores such as frailty, porcelain aorta, sequelae of chest radiation), the decision between SAVR and TAVI should be made by the Heart Team according to the individual patient characteristics, with TAVI being favoured in elderly patients suitable for transfemoral access

IMAGING PRIOR TO TAVI

Necessary things to know preprocedural of any TAVI

1- Cardiac gated CTA with femoral runoff
2- High quality TEE/TTE
3- Evaluation of Coronary disease/angiogram

The cardiac gated CT angiogram is used to determine critical measurements needed to size and place the valve. Edwards products determine the valve size based on AV area, while Medtronic products determine the size of perimeter. Both take measurements in systole[35]

Important measurements include

1- Annular size
2- Sinuses of Valsalva
3- Coronary heights
4- Sinotubular junction
5- Mid ascending aorta
6- LV outflow tract
7- Coplanar delivery angle

The AV annulus is measured at the nadir of each of sinus. Its elliptical shape must be determined at this position by careful outlining with reconstruction software. The sinuses of Valsalva are measured at point in which sinuses are widest. Each of the three sinuses are measured from widest point of sinus to opposing valve commissure. The coronary height needed to safely position a transcatheter valve is generally 1 cm. It is measured from nadir of sinus to inferior aspect of coronary ostium. When evaluating coronary heights, it should be related to the size of the sinuses of Valsalva, as larger sinuses allow increased room between valve and coronary ostia at any given coronary height. Coronary heights of 1 cm and sinuses over 3 cm generally will not cause coronary obstruction. LVOT and STJ height also need to be quantified. The LVOT is measured 3 mm below the annulus, an LVOT diameter of less than 2 cm should raise concern for possible device embolization. When evaluating the annulus on CTA, it is necessary to determine the coplanar axis at which the three nadirs of the annulus are in the same flat plane. This angle will provide the view at which device

should be deployed. Heavy annular or LVOT calcium will increase the risk of stroke, annular rupture and paravalvular leak. A horizontal heart is an angle between the perpendicular plane of the AV annulus and a horizontal reference line <30 degree. Abdominal and pelvic vasculature should be determined to plan vascular access. A heavily calcifies or torturous artery should be avoided for device access.

Preprocedural echocardiogram for valve area, gradient, insufficiency, anatomy and degree of calcification should be done.

Coronary angiogram should be obtained in all patients prior to atvi and managed accordingly. Cardiac catheterisation in case of inconsistent values on echo will help to confirm the diagnosis. The peak to peak gradient obtained on cardiac catheterisation is 70% of peak instantaneous gradient obtained on echocardiogram, while mean gradient is slightly smaller than peak to peak gradient.

VALVE SIZING

Annulus Sizing		20 mm	23 mm	26 mm	29 mm
Native Valve Annulus Size (CT)	Area	273 - 345 mm^2	338 - 430 mm^2	430 - 546 mm^2	540 - 683 mm^2
	Area Derived Diameter	18.6 - 21 mm	20.7 - 23.4 mm	23.4 - 26.4 mm	26.2 - 29.5 mm
Native Valve Annulus Size TEE		16 - 19 mm	18 - 22 mm	21 - 25 mm	24 - 28 mm

	Valve size	Aortic annulus measurements		Sinus of valsalva diameter	Sinus of valsalva height
		Diameter	Perimeter		
Evolut™ PRO and Evolut™ R valves	23 mm	17†/18–20 mm	53.4†/56.5–62.8 mm	≥ 25 mm	≥15 mm
	26 mm	20–23 mm	62.8–72.3 mm	≥ 27 mm	≥15 mm
	29 mm	23–26 mm	72.3–81.7 mm	≥ 29 mm	≥15 mm
Evolut™ R valves	34 mm	26–30 mm	81.7–94.2 mm	≥ 31 mm	≥16 mm

Fig 4-VALVE SIZING- TOP-EDWARD SAPIEN; BOTTOM- EVOLUTE R

VALVE IMPLANTATION

Anaesthesia- Procedure can be done under general anaesthesia or conscious sedation. General anaesthesia is preferred if a TEE is performed simultaneously.[36] Concept of minimalist TAVI has been favoured recently which includes moderate sedation, percutaneous access and post implantation TTE.[37]

Infection and antithrombotic prophylaxis- IV antibiotics are given on call and continued for 48 hours (Vancomycin or cefazolin). Aspirin(160-325 mg) and clopidogrel(300 mg) are administered at least 24 hours prior to procedure

Access- Arterial access is obtained for aortic angiography with a 5- to 6-Fr pigtail catheter and a venous sheath is inserted for RV pacing. The contralateral artery is cannulated percutaneously or by surgical cutdown. Preclosing with suture mediated device is regularly performed. [38]

Crossing the valve- Once anticoagulated with heparin (100u/kg) the native aortic valve is crossed using Amplatz AL2 catheter and a straight guidewire, The preshaped extra stiff Amplatz .035 inch , 270 cm lengh guidewire (Safari/Confida) is exchanged through the AL 2.

Balloon aortic valvuloplasty- BAV is performed under rapid ventricular pacing using Retroflex balloon (20,23,25 balloon for 23,26,29 prosthesis). Patients with favourable anatomy BAV may not be required.

Delivery sheath insertion- With guidewire in aorta, the previously inserted 8 F sheath is removed and dilation of artery is performed, after which delivery sheath is inserted.

Balloon expandable valve insertion and deployment

In the predetermined reference projection valve is positioned in the centre of annulus and positioned 3-5 mm below the annulus. When deployed ideally 80-90% of valve will be on aortic side and 10-20% ventricular. After confirmation of position, valve is deployed under rapid pacing at 180-220 bpm. Gradients and paravalvular leaks are assessed post deployment.

Self expanding valve deployment

Core valve is positioned 4 mm deep which is about 0.5 diamond or one ring, below the annulus. Valve position is assessed with pigtail injection and after confirmation of adequate position it can be released. Once flared valve touches the annulus, rest of the valve can be deployed under moderate pacing (100-120 /min) until 2/3rd of valve

is released. In case of unsatisfactory position valve can be taken back into sheath and repositioned at this point.

CHALLENGES

Structural valve deterioration- It is defined as permanent intrinsic changes of valve including calcification, pannus and leaflet failure leading to valve dysfunction. The risk is heavily influenced by valve design and patient age.

Subclinical leaflet thrombosis- Identified on CT imaging in 10-15% of TAVI patients. It is seen as hypoattenuated leaflet thickening (HALT) and reduced leaflet motion (RELM), which correlates with thrombus.[39] Risk factors not clearly defined but regional stent under-expansion has been associated with increased risk of leaflet thickening. Oral anticoagulation seems to prevent and resolve the phenomenon

Stroke- Stroke has been associated with 5-10 fold increased risk of short term mortality. Maximum chances are during the valve positioning and deployment. The role of antiplatelet and OAC to prevent stroke following TAVI is ill defined.

Permanent pacemaker implantation- Conduction disorder result mainly form mechanical compression of valve or calcified native aortic valve to the closely lying bundle of His. Newer LBBB or VHB necessitating pacemaker implantation is seen in 5-35% of patients.[40]

Access site complications- Transfemoral is the safest and simplest vascular access route and is associated with improved outcomes compared to other approaches. Facilitated by smaller delivery systems, valve delivery is achievable in 90% of cases and incidence of major complications has reduced to <2% in contemporary practice.

Infective endocarditis- IE affects 0.5-3% of patients within first year of procedure.[41] TAVI related endocarditis is caused mostly by Enterococcus species. Rigorous sterility is of paramount importance. Xeltis valve which is a bioabsorbable polymer scaffold which is endothelised and replaced by recipient tissue is in preclinical development and may reduce the risk of bacterial adherence and consequent endocarditis.[42]

EXPANDING INDICATIONS

Valve in valve- TAVI has been increasingly used to treat failed surgical aortic bioprosthesis. Imaging is very important for accurate sizing, where inner diameter of

the bioprosthesis should be considered as the annulus size. Risk of coronary obstruction is higher in Valve in valve TAVR of upto 3.5%. Procedures like Chimney stenting and BASILICA procedure have been introduced as a bail out for coronary obstruction after TAVI.[43,44] Also the mean gradients post VIV TAVI are higher than native valve TAVI secondary to patient prosthesis mismatch. Frame fracture is being performed for the severe patient prosthesis mismatch in such patient showing good outcomes.

Table 3- AHA 2020 guideline for Valve in Valve TAVR[33]

Class	Indication
2a	For severely symptomatic patients with bioprosthetic aortic valve stenosis and high or prohibitive surgical risk, a transcatheter ViV procedure is reasonable when performed at a Comprehensive Valve Center
2a	For patients with severe HF symptoms caused by bioprosthetic valve regurgitation who are at high to prohibitive surgical risk, a transcatheter ViV procedure is reasonable when performed at a Comprehensive Valve Center

Bicuspid aortic valve

Bicuspid aortic valve was exclude from majority of clinical trials in TAVR. Bicuspid valves tend to have bulky calcium, higher hinge point, asymmetric annulus and a dilated aorta which may complicate TAVI outcomes. Classification including Sievers classification and Jilaihawi radiological classification provide insight into the anatomical details and help in further planning.[45] Early generation valves had high paravalvular leak after valve implantation for bicuspid valve , which has now decreased from 8.5-14.7% to 0-2.7% with the use of newer generation valves.

Table 4- AHA 2020 Guidelines for TAVR in Bicuspid Aortic valve[33]

Class	Indication
2b	In patients with BAV and symptomatic, severe AS, TAVI may be considered as an alternative to SAVR after consideration of patient-specific procedural risks, values, trade-offs, and preferences, and when the surgery is performed at a Comprehensive Valve Center

AORTIC REGURGITATION

The main challenge during TAVI for native pure aortic valve regurgitation is absence of annular and leaflet calcium which is necessary for device anchoring. The lack of calcium , increased stroke volume secondary to severe AR and presence of aortic root dilation makes device positioning and deployment very difficult with risk of embolisation and malposition with increased paravalvular regurgitation.[46] Newer generation valves have been found to have better outcomes compared to old generation ones but currently not recommended for pure AR. Jena valve which has clipping mechanism to hold the valve and doesn't need calcium, has received FDA designation of breakthrough device for severe AR. ALIGN-AR EFS trial is studying the outcomes in post TAVI with Jena valve in severe AR and study is expected to complete by 2026.

Table 5- AHA 2020 Guidelines for TAVI in AR [33]

Class	Indication
3-Harm	In patients with isolated severe AR who have indications for SAVR and are candidates for surgery, TAVI should not be performed

MODERATE AS WITH LV DYSFUNCTION

It is defined by a mean transaortic gradient between 20 and 40 mmHg and an aortic valve area between 1.0 and 1.5 cm2 in patients with LVEF lower than 50%. In this population the reduction in LVEF is thought to be secondary to non valvular cause and was thought that TAVR will help to unload ventricle and improve outcomes. TAVR UNLOAD trial (NCT02661451), which is an international, multicenter, randomized, open-label, clinical trial comparing TAVR using the Edwards Sapien 3 valve in addition to optimal heart failure therapy with optimal heart failure therapy alone in patients with moderate AS and reduced LVEF.

ASYMPTOMATIC SEVERE AS

As many as 50% of patients with severe AS report no symptoms at time of diagnosis and optimal timing of intervention in such cases is debated. Retrospective data suggest strategy of early AVR in assymptomatic patients is associated with improved survival though no randomised trial exist. EARLY TAVR trial is looking into such group of patients comparing TAVR with regular surveillance.

STUDY HYPOTHESIS

In patients with high to intermediate risk for surgery, TAVI has been suggested to have good outcomes in the Indian subpopulation.

OBJECTIVES

Primary objective

To obtain the early and late outcomes after TAVI including mainly mortality and MACE events.

Secondary objective

- To obtain data on baseline characteristics, complications and further followup outcomes after TAVI.
- To study the factors affecting the procedural outcomes

STATISTICAL ANALYSIS

The analysis is performed using SPSS statistical software

- Categorical variables were presented as proportions and continuous variables were presented as mean with standard deviation.
- Chi-square test was used for determining association between categorical variables.
- Comparison pre and post TAVI was done using the **Wilcoxon signed rank test.**
- **Mann-Whitney test** was used for comparing the non parametric continuous variable with final outcome.
- **Kaplan-Meier survival** curves to assess differences between groups for the time to an event data.
- Univariate analysis was performed for various factors to find any association with primary and secondary outcomes

MATERIALS AND METHODS

It's a retrospective and prospective observational study of all patients undergoing TAVI from 2017 until December 2020. Followup of all patients was done at 1 month and 1 year. Patients who underwent TAVI in 2020 mid and later part, didn't have one year followup as the study period was upto December 2020. Total 23 patients underwent TAVI until December 2020. All patients followup data upto one year is available. One year followup data of 18 patients is available due to time constraints. Data was collected retrospectively of patients prior to 2018 using the electronic medical records and prospectively after that.

- **Inclusion**- Based on the Surgical risk involved patients were selected for TAVR. All patients who underwent TAVR were included in study
- **Exclusion**- No specific exclusion criteria

Patient preprocedural, procedural and post procedural characteristics were obtained. Detailed proforma has been attached. Patient primary outcome studied is mortality and the MACE events which included combined mortality or heart failure or myocardial infarction or stroke. Other outcomes included heart failure hospitalization, need for pacemaker implantation, other procedural and postprocedural complications including valvular degeneration, valvular thrombosis, paravalvular leak and access site complications.

Preprocedural evaluation included baseline demographics including age, risk factors like diabetes, hypertension, dyslipidemia. Risk score for aortic valve implantation was evaluated using the STS risk score and euro score 2. Mainly patients with intermediate to high risk were included in study. Also patients who were frail, with porcelain aorta or history of previous cardiac surgery, radiation were considered for TAVI. Baseline echo and ecg parameters were included. CT evaluation included valve details like annulus size, sinus diameter, aorta size, coplanar angle, coronary height and access site diameter were included.

Procedural characteristics included type of valve, size used, cardiac catheterization details, peak to peak gradient and amount of aortic regurgitation. Post procedure gradient and residual paravalvular leak were studies including the need for pre and post balloon dilation. Post procedural and hospital stay complications were recorded including new conduction disturbances with need for pacemaker implantation, stroke, acute coronary event and access site complications and need for emergency surgery. Patients were followed up for upto one month and one year. Followup data included symptomatic status, ecg and echocardiographic parameters and any hospital admissions. Additional complications like valve leaflet thrombosis, patient prosthesis mismatch, need for PPI were recorded over followup period.

RESULTS

Total 23 patients underwent transcatheter aortic valve implantation from 2017 to end of 2020. All patients were followed up for upto 1 year. Those patients who underwent TAVI in 2020 had followup data upto one month, that includes 18 patients.

Baseline characteristics

Age of presentation ranged from 60 to 88 years with 69.6% being males. Mean BMI was 25.5 kg/m2. Risk factors included Hypertension in 78.3%, dyslipidemia in 52.1% and diabetes in 34.8%. Chronic lung disease was seen in 43.5% which is an important component of surgical risk assessment. 26.1% were frail as assessed with frieds criteria for frailty, previous radiation therapy was done in one patient post breast cancer chemoradiotherapy and porcelain aorta was seen in 2(8.7%). 11 patients had history of prior openheart surgery including coronary artery bypass grafting, bioprosthetic aortic valve replacement and mechanical prosthesis at mitral position.

Table 6- Baseline demographics

Baseline demographics	
AGE(years)	60-88(74)
GENDER	MALE- 16(69%) FEMALE – 7(30.4%)
BMI(kg/m2)	25.5 (+/- 3.96)
FRAILTY	6 (26.1%)
DIABETES	8(34.8%)
HYPERTENSION	18(78.3%)
DYSLIPIDEMIA	12(52.1%)
COAD	10(43.5%)
STROKE	1(4.3%)
PERIPHERAL ARTERIAL DISEASE	4(17.4%)
CKD	2(8.7%)
PORCELAIN AORTA	2(8.7%)

Baseline demographics	
PREVIOUS MI	6(26.1%)
PREVIOUS PCI	3(13%)
PREVIOUS CABG	7(30.4%)
PREVIOUS BAV	0%
PREVIOUS AVR	3(13%)
PREVIOUS MVR	1(4.3%)
PREVIOUS RADIATION	1(4.3%)

Symptoms of presentation ranged from heart failure admission to NYHA functional class 3 dyspnoea, while some had syncope as the predominant symptom of presentation. Median NT pro BNP value was 3050 pg/ml.

Table 7- Baseline symptoms and blood investigations

Symptoms		Blood investigations	
HISTORY OF HEART FAILURE HOSPITALISATION	39.1% (9)	Hb (gm/dl)	12.45 (9.8-15.9)
		CREATININE(mg/dl)	1.1 (0.54-1.55)
SYNCOPE/PRESYNCOPE	13% (3)	NT PROBNP(pg/ml)	3050 (342-20000)
NYHA	IV-39.1%(9) III- 39.1% (9) II- 21.7% (5)	SERUM ALBUMIN(g/dl)	3.9 (2.2-4.9)
		SERUM PROTEIN(gm/dl)	7.4 (5.2-8.3)

Surgical risk score- Mean STS risk score for mortality for aortic valve replacement was 5.5 +/-1.88, while Euroscore2 was 7.6 +/-5.24. There were 88.7% in either STS or Euroscore2 score of > 4%.

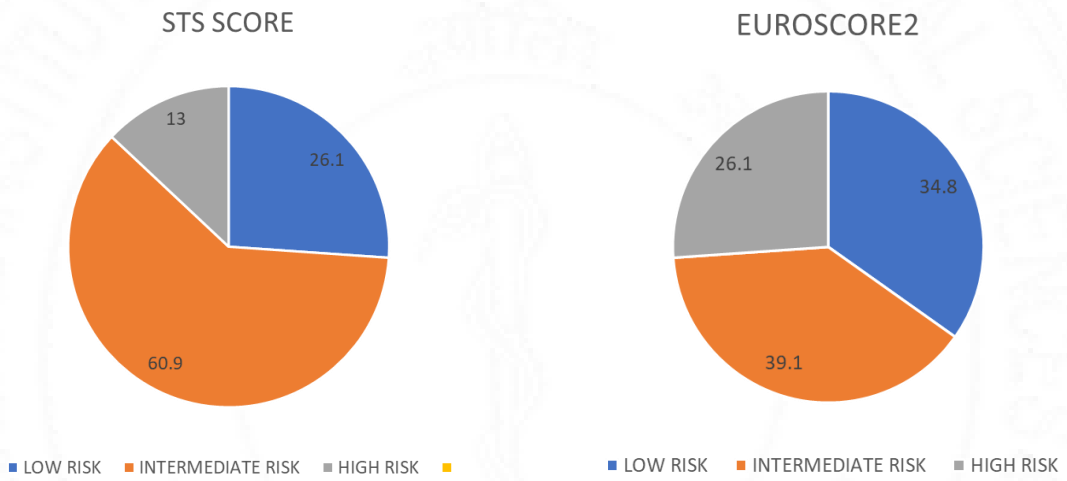

Fig 5- STS and Euro score 2

Coronaries- Coronary were assessed prior to planning for TAVI procedure. 14(60.9%) patients had normal coronaries while 3(13%) patients underwent PCI for significant coronary lesion.

Table 8- Coronary artery disease

Coronary status	
NORMAL	14(60.9%)
SINGLE VESSEL DISEASE	2(8.7%)
DOUBLE VESSEL DISEASE	1(4.3%)
POST CABG- PATENT GRAFTS	2(8.7%)
POST CABG WITH OCCLUDED SVG GRAFT	4(17.4%)

Echo- Aortic valve area ranged from 0.3 cm2 to 2.1cm2 with median area of 0.7cm2. One (4.3%) patient had severe left ventricular dysfunction with low flow low gradient severe aortic stenosis confirmed on dobutamine stress echocardiography. One patient had native pure aortic valve regurgitation with no aortic stenosis. Moderate aortic stenosis with severe aortic regurgitation was seen in 1(4.3%) while severe aortic regurgitation was seen in 4(17.4%) patients. 2(4.3%) patients had rheumatic etiology with mild mitral valve gradients.

Table 9- Echocardiographic parameters

Echo parameters	
EJECTION FRACTION	57.43 +/- 14.9% (31-86%)
NORMAL LV FUNCTION	13(56.5%)
MILD LV DYSFUNCTION	7(30.4%)
MODERATE LV DYSFUNCTION	2(8.7%)
SEVERE LV DYSFUNCTION	1(4.3%)
AS SEVERITY(mm Hg)	0-85 (46 +/-19.8)
NO AS	1(4.3%)
MODERATE AS	1(4.3%)
SEVERE AS	15(65.2%)
CRITICAL AS	6(26.1%)
AR SEVERITY	
NONE	1(4.3%)
TRIVIAL	6(26.6%)
MILD	6(26.6 %)
MODERATE	6(26.6%)
SEVERE	4(17.4%)

Echo parameters	
PULMONARY HYPERTENSION	
NORMAL	8(34.8%)
MILD	10(43.5%)
MODERATE	2(8.7%)
SEVERE	3(13%)
MS	
NONE	21(91.3%)
MILD	2(8.7%)
MITRAL REGURGITATION	
NONE	3(13%)
TRIVIAL	4(17.4%)
MILD	9(39.1%)
MODERATE	7(30.4%)

Ecg- Two (8.7%) patients had baseline atrial fibrillation , while one patient had typical atrial flutter. Baseline complete left bundle branch block was seen in 21.7% while complete right bundle branch block in 13%.

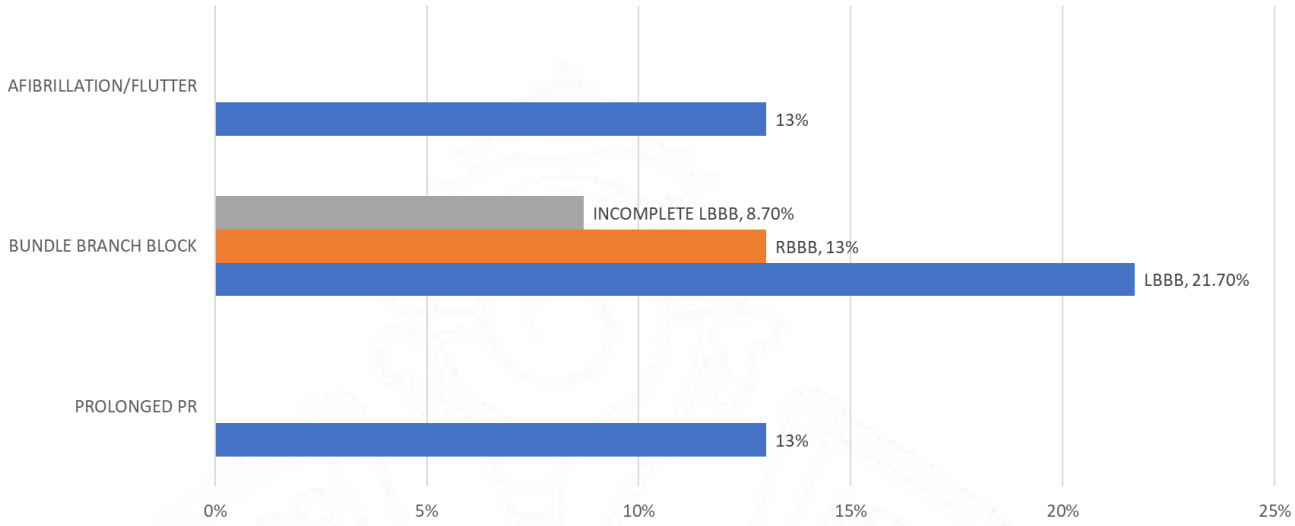

Fig 6- Baseline ECG findings

ETIOLOGY- Majority had degenerative etiology while 2(8.7%) patients had rheumatic etiology.

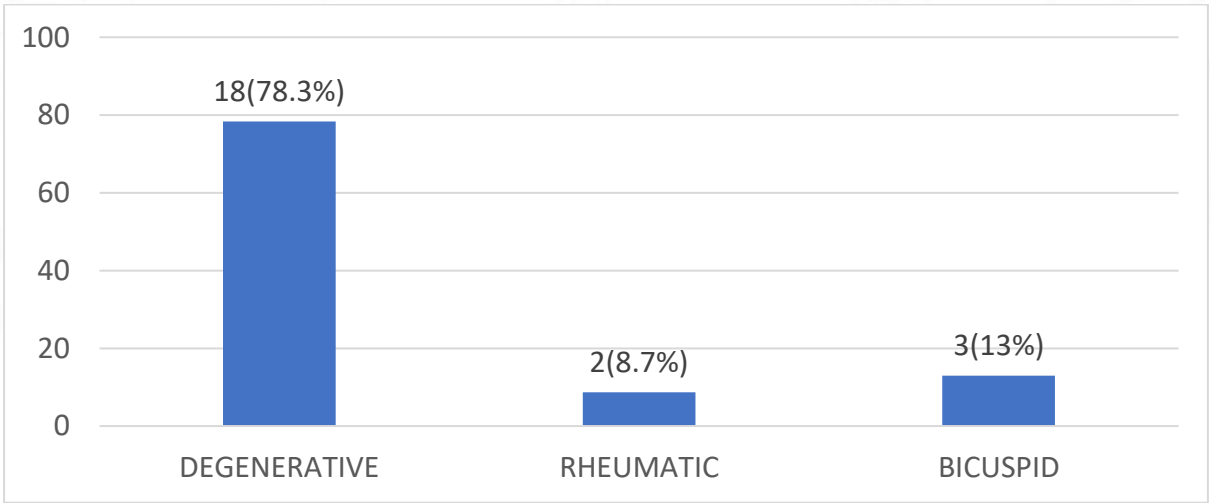

Fig 7- Etiology of valvular disease

Patients with bicuspid aortic valve , native valve pure aortic regurgitation, degenerated bioprosthesis and low flow low gradient severe aortic stenosis were also included and

underwent TAVI in view of high surgical risk, though surgical valve replacement is still the preferred mode of treatment as per guidelines.

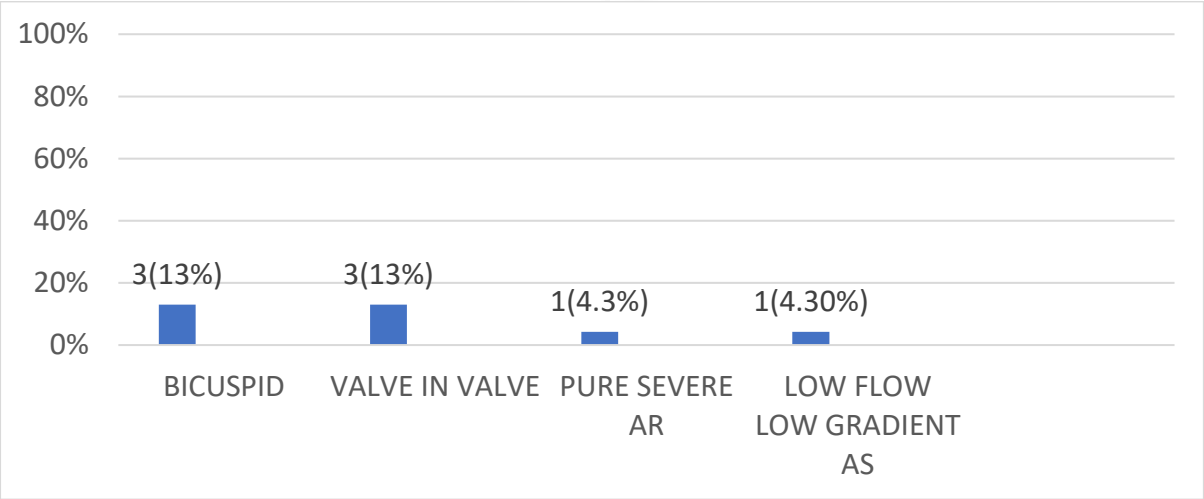

Fig 8- Indication except non trileaflet degenerative valve

CT parameters

Mean aortic annulus diameter was 24.08 +/-3.04 mm, while mean aortic annulus perimeter was 69.57+/-7.7 mm. Mean Sinus diameter was 31.89 +/-4.87 mm. Coronary heights were 14.86 +/- 3.9 for right coronary while 13.77 +/- 3.3 mm for left coronary. Peripheral arteries were assessed for size, tortorousity, calcification or any occlusion.

Table 10- CT parameters

CT PARAMETERS	
PERIMETER(mm)	69.57 +/- 7.7 (58-86)
ANNULUS DIAMETER(mm)	24.08 +/- 3.04 (18-29)
ANNULUS AREA(cm2)	3.67 +/- 0.63 (2.57-4.54)
SINUS DIAMETER(mm)	31.89 +/- 4.87 (19 -40)
SINOTUBULAR JUNCTION(mm)	28.89 +/- 4.6 (23-38)
ASCENDING AORTA(mm)	34.55 +/- 5.5 (23-45)

Table 11- Coronary height from CT

CORONARY HEIGHT	
RIGHT CORONARY(mm)	14.86 +/- 3.9 (7.3 -24)
LEFT CORONARY(mm)	13.77 +/- 3.3 (9.69-20.9)

Table 12- Peripheral access site artery diameter

PERIPHERAL ARTERIAL DIAMETER	RIGHT	LEFT
COMMON ILLIAC(mm)	9.79 +/-1.4 (6.3-13)	9.55 +/-1.39 (6.2-12.6)
EXTERNAL ILLIAC(mm)	7.42 +/- 1.09 (5.2-9.4)	7.41 +/- 1.09 (5.1- 9)
COMMON FEMORAL(mm)	8.13 +/-1.38 (5.6-11.1)	7.77 +/- 1.22 (6.1- 11.1)

HEMODYNAMICS

Mean value of LV end diastolic pressure was 19.8 +/-9.6. Peak to peak gradient value was 49.2+/-31 mm Hg, while mean pressure gradient was almost similar to peak to peak gradient i.e. 46.3 +/- 28 mm Hg. Severe AR was seen in 4(17.4%) patients.

Table 13- Hemodynamic parameters from cardiac catheterisation

Hemodynamic Data	
LV SYSTOLIC PRESSURE(mm Hg)	170 +/- 31 (120-220)
LV END DIASTOLIC PRESSURE(mm Hg)	19.8+/-9.6 (6-48)
AORTIC SYSTOLIC PRESSURE(mm Hg)	119.3 +/- 22.36 (90-164)
AORTIC DIASTOLIC PRESSURE(mm Hg)	49.1 +/- 15.5 (30-70)
PEAK TO PEAK PRESSURE GRADIENT(mm Hg)	49.2 +/- 31 (0-139)
MEAN PRESSURE GRADIENT(mm Hg)	46.3 +/-28 (0-120)
AORTIC REGURGITATION MILD MODERATE SEVERE	 7(30.4%) 3(13 %) 4(17.4%)

PROCEDURAL CHARACTERISTICS

16 (69.9%) underwent TAVI using self-expanding 3rd generation Evolute R, while balloon expandable valve in form of Edward Sapien 3 was done in 2(8.7%) and MyVal was used in 5(21.7%). Majority valve sizes ranged between 23-29.

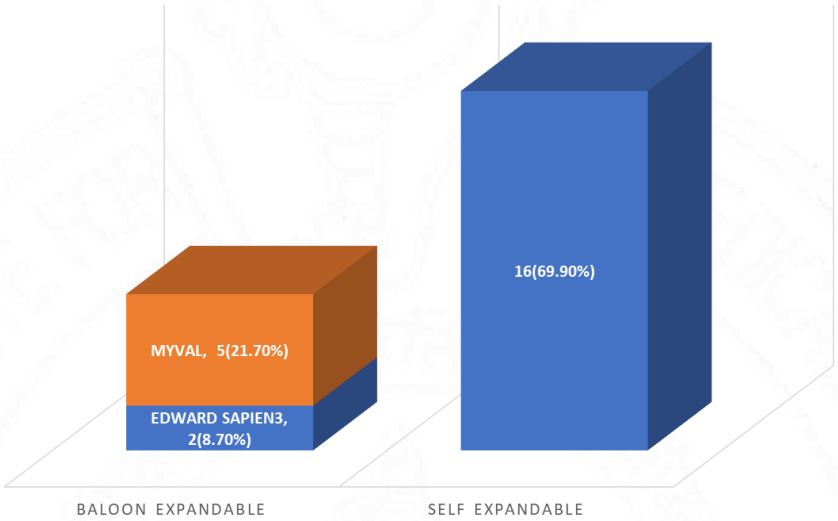

Fig 8 – Type of valve used in study

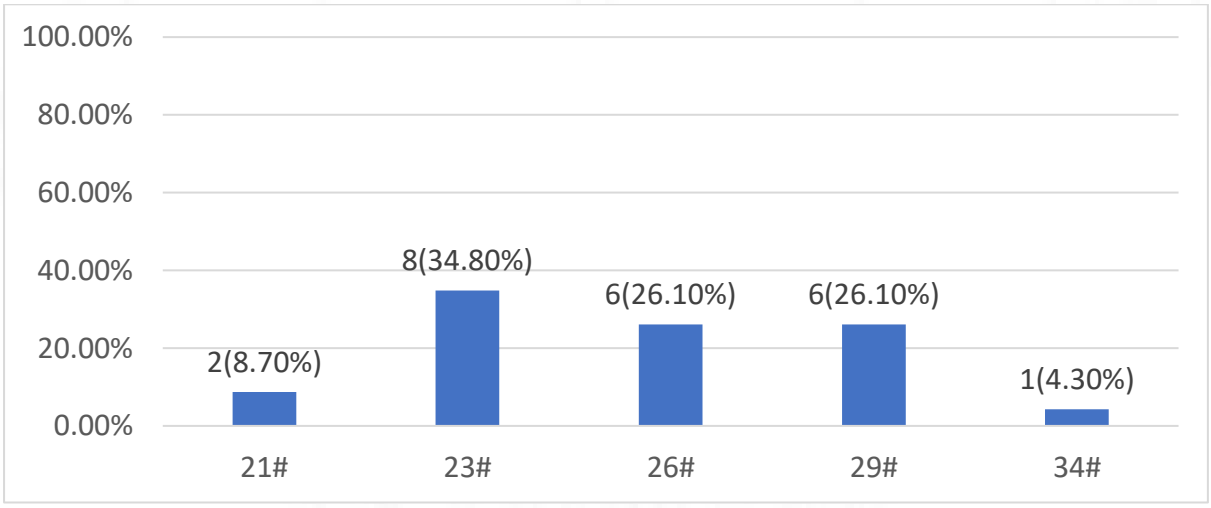

Fig 9- Valve sizes used

All cases were done in general anaesthesia using femoral access. Predilation was done in 18(78.3%) while post dilation was done in 6(26.1%) mainly in view of post implantation significant aortic regurgitation. None of the patient had significant gradient or aortic regurgitation post valve implantation.

Table 14- Procedural characteristics

TAVI Procedural Characteristics	
ACCESS FEMORAL	 23(100%)
ANAESTHESIA GENERAL	 23(100%)
PREDILATION	18(78.3%)
POST DILATION	6(26.1%)
POST GRADIENT 0-10 MM HG 11-20 MM HG	 19(82.6 %) 4(17.4 %)
POST AR NONE TRIVIAL MILD	 7(30.4%) 11(47.8%) 5(21.7%)

Complications

Post TAVI conduction defects were seen mainly in form of LBBB and complete heart block. CHB was seen in all patients with preexisting right bundle branch block. One patient had transient CHB which recovered while 2(8.7%) patients underwent permanent pacemaker implantation. All access site closure were done using proglide suture. Access site complications were seen in 6(26.6%), of which 2(8.7%) patients needed surgical intervention. One patient had arterial rupture for which he underwent covered stent implantation but in view of acute thrombosis of stent underwent iliofemoral bypass grafting. Second patient had acute arterial occlusion due to proglide suture across the posterior arterial wall which was immediately repaired. 1(4.3%) patient had hypotension and cardiac arrest post anaesthesia after which he was successfully revived but had a prolonged hospital course with acute renal dysfunction which subsequently improved.

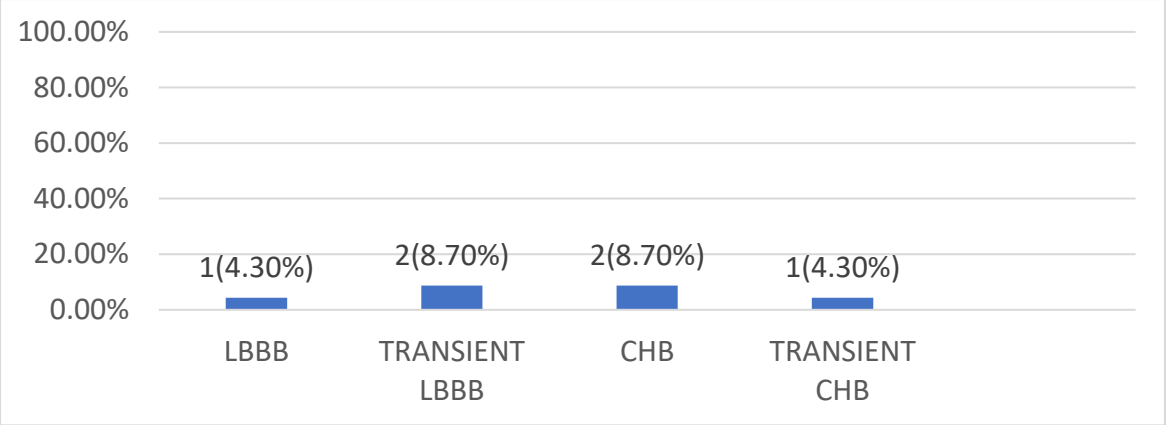

Fig 10- Post TAVI conduction abnormalities

Table 15- Access site complications

ACCESS SITE COMPLICATIONS	6(26.6%)
HEMATOMA	1(4.3%)
ARTERIAL DISSECTION	1(4.3%)
ARTERIAL OCCLUSION	2(8.6%)
ARTERIAL RUPTURE	1(4.3%)
PSEUDOANEURYSM	1(4.3%)

Hospital Course

Mean NT proBNP levels post TAVI were 2075+/-1900 pg/ml which is significantly lower than preTAVI values. There was no mortality, acute coronary event or worsening of heart failure symptoms post procedure. There was no valve embolization or aortic complications. 3(13%) patients had stroke of which one patient had transient ischemic attack while two patients had disorientation post procedure which on further evaluation were found to have multiple infarcts.

Table 16- Post TAVI- Hospital stay

Post TAVR demographics		
POST –TROP T(PG/ML)	33.5 (230-0)	
POST NT PROBNP(PG/ML)	2075+/- 1900 (278-8000)	(p- .001)
LENGTH OF HOSPITAL STAY(DAYS)	7 (5-16)	
SYMPTOM WORSENING	0%	
POST MI	0%	
POST MORTALITY	0%	
POST STROKE TIA CVA	3(13%) 1(4.3%) 2(8.7%)	
RENAL DYSFUNCTION	1(4.3%)	
PROLONGED VENTILATION(>24 HOURS)	1(4.3%)	
BLOOD TRANSFUSION	6(26.1%)	
TACHY-ARRYHTMIA	0%	
EMERGENCY SURGERY	0%	

FOLLOWUP HEMODYNAMICS

All patients were followed up where 5 procedures were done in 2020 so followup data of these is available upto 1 month. At 1 month followup majority were in NYHA I-II, while 1(4.3%) patient with valve in valve TAVI had patient prosthesis mismatch with severely elevated prosthetic valve gradient. Patient was admitted with heart failure and subsequently underwent native valve frame fracture. Mean prosthetic valve gradient post TAVI was significantly lower with no patient having more than mild aortic regurgitation.

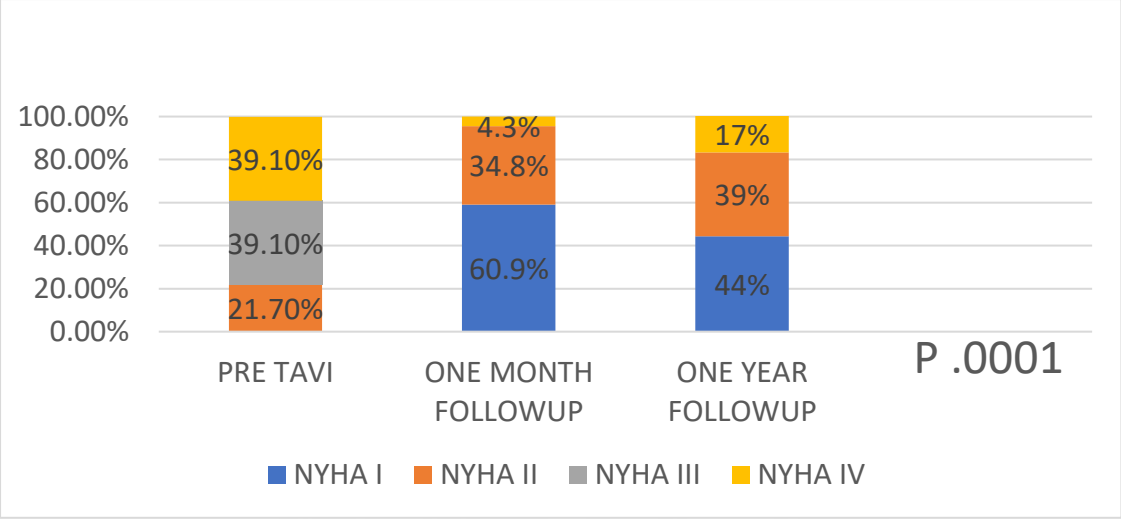

Fig 11- Followup NYHA class

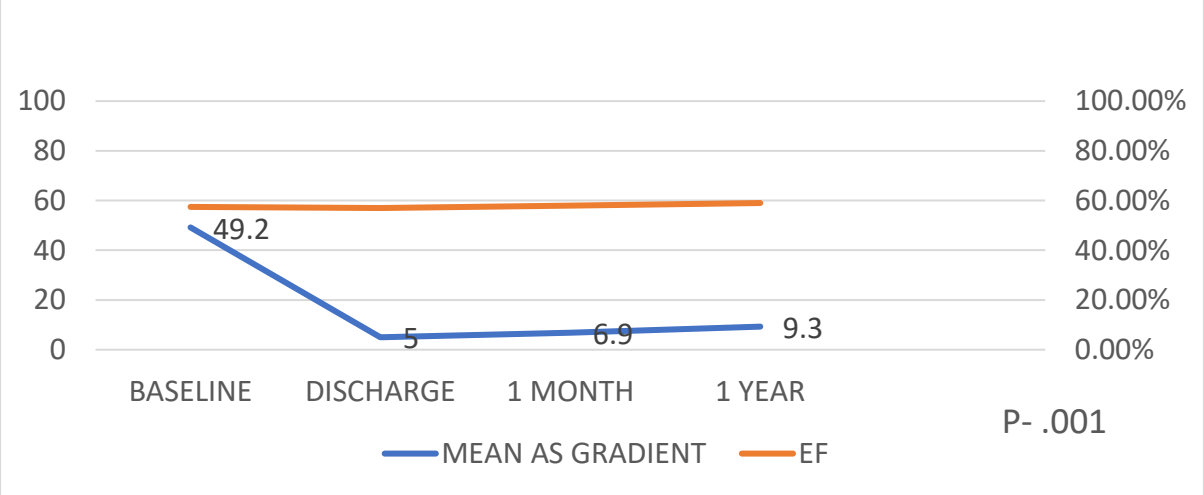

Fig 12- Followup aortic valve gradients

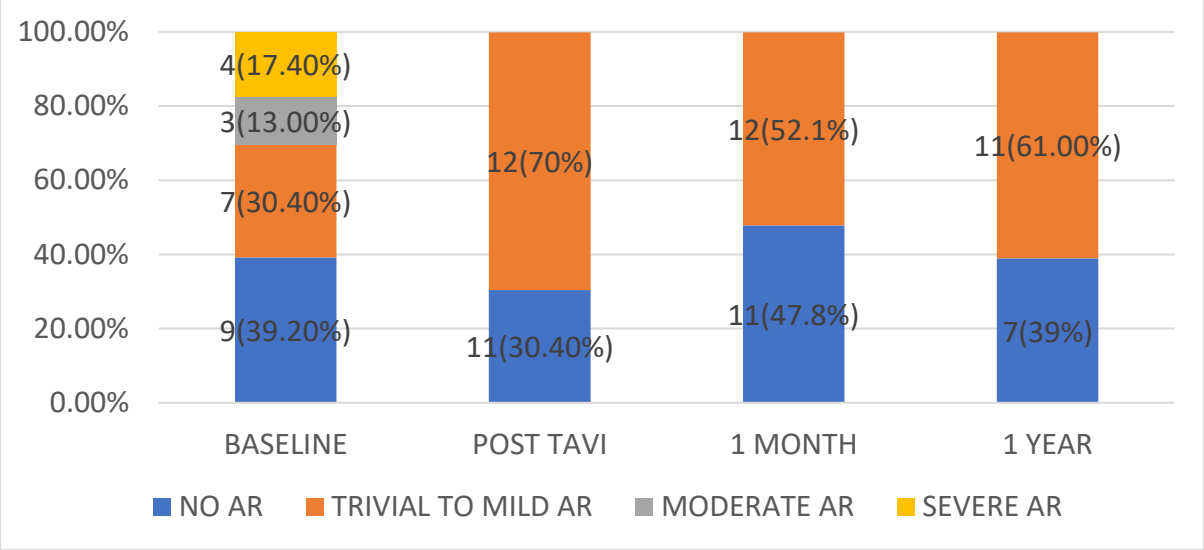

Fig 13- Followup aortic valve regurgitation

During one month to one year followup period there was no mortality, no ACS or CVA. 3(16.7%) patients had heart failure admission predominantly secondary to diastolic dysfunction. 2(11%) patients had leaflet thrombosis detected in view of moderately elevated valve gradients and further confirmed by CT. Likely cause was non compliance to antiplatelet drugs. One patient was started on iv heparin after which mean gradients decreased from 29 to 14 mm Hg and both were continued on oral anticoagulants. 1(5.6%) patient had holter documented long sinus pause of 6.8 sec after which pacemaker implantation was done. 1(5.6%) patient who underwent post TAVI iliofemoral bypass grafting for arterial rupture had graft occlusion with critical limb ischemia after which patient had to undergo limb amputation.

Table17- Complications during followup

	1 MONTH(23 patients)	1 YEAR(18 patients)
ACS	0	0
CVA	0	0
PATIENT PROSTHESIS MISMATCH	2(8.7%)	0
VALVE THROMBOSIS	0	2(11%)
ARRHYTHMIA SICK SINUS SYNDROME	0	1(5.6%)
HF ADMISSION	1(4.3%)	3(16.7%)
OTHER COMPLICATIONS FOOT GANGRENE-LIMB AMPUTATION	0	1(5.6%)
MORTALITY	0	0
DRUG COMPLIANCE	100%	16(88.8%)

Overall outcomes

At the end of one year there was no mortality. 4(17.3%) patients had heart failure hospitalization. Other complications included prosthetic valve mismatch in 2(8.6%), prosthetic valve thrombosis in 2(8.6%), pacemaker implantation in 3(13%), stroke in 3(13%) and access site complications needing surgical intervention in 2(8.7%). MACE event was defined by mortality or heart failure hospitalization or MI or stroke. By end of one year the cumulative MACE events were seen in 38%.

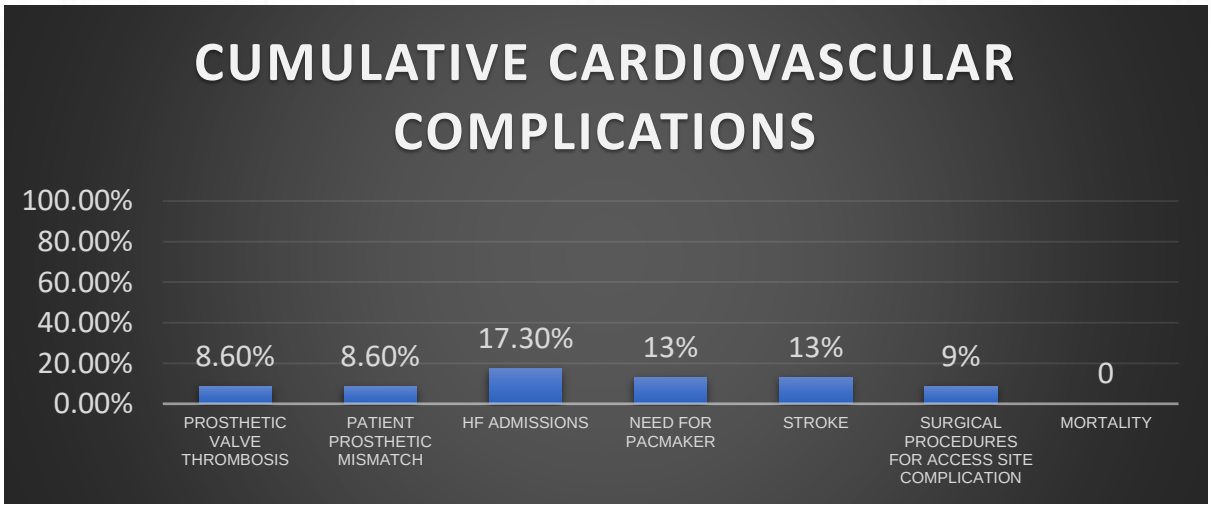

Fig 14- Cumulative outcomes

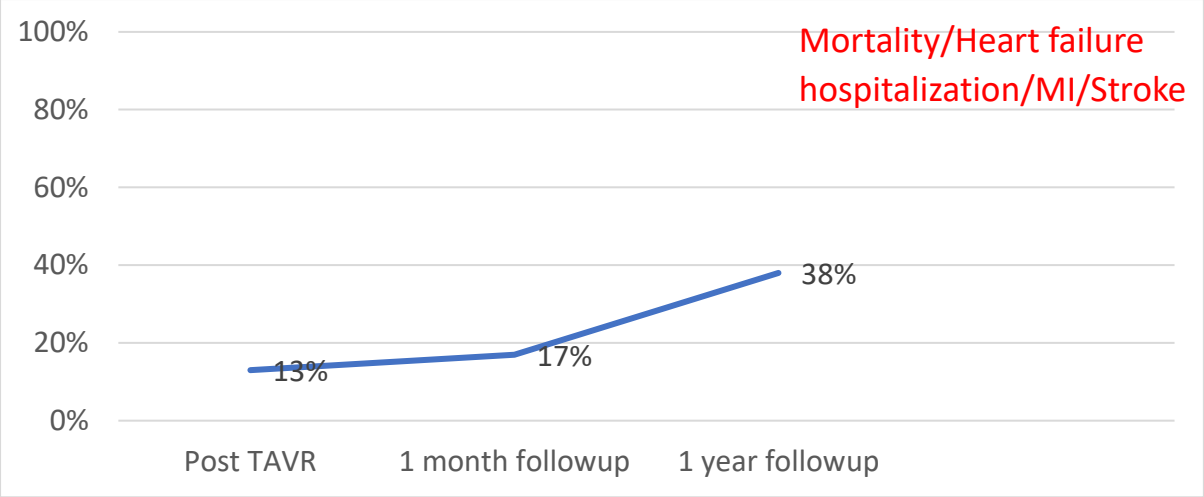

Fig 15- Cumulative MACE events

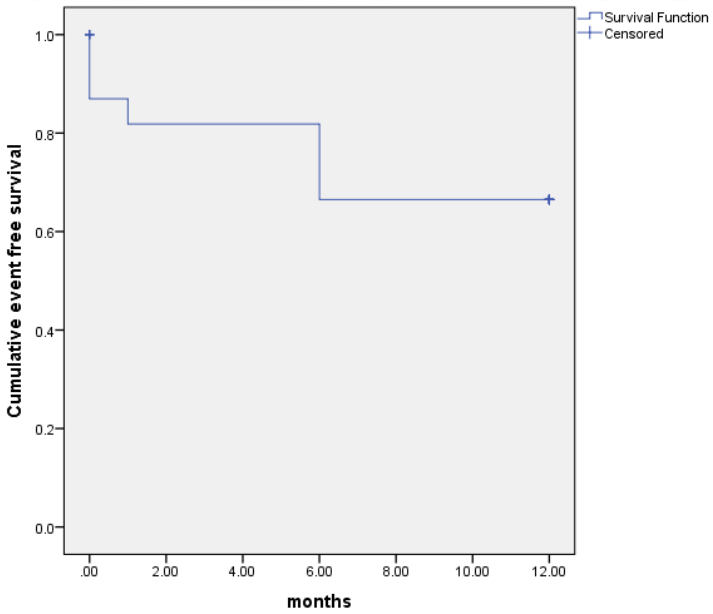

Fig 16- Event free survival

Secondary analysis

Balloon vs self expandable valve- No significant difference was noted with respect to need for postdilation, post implantation AS/AR, need for pacemaker implantation or stroke

Table 18- Balloon vs self expandable valve

	BALLOON EXPANDING	SELF EXPANDING	P VALUE
POSTDILATION	42%	18%	.376
POST GRADIENT >10 mm	28%	12%	.579
POST AR(mild)	14%	25%	.452
COMP HEART BLOCK	14%	6%	.922
ACCESS COMPLICATION	28%	25%	.922
STROKE	0	18%	.492

Need for pacemaker- Baseline RBBB was found to be significantly associated with need for pacemaker implantation. All patients with underlying RBBB had transient or permanent complete heart block. No difference was seen for need for pacemaker implantation with respect to pre or post balloon dilation, prosthesis size or type of prosthesis.

Table 19- Factors predicting need for pacemaker implantation

Parameters	P value
Predilation	.328
Post dilation	.759
PR PROLONGATION	.619
Bundle branch block(RBBB)	.001
Arrhyhtmia	.644
Prosthesis size	.573
Annulus diameter	.931
Prosthesis type	.772

Factors affecting final cumulative MACE

Various factors were compared with the final total mace events. No factor was found to be significantly associated with final cumulative MACE event.

Table 20- Factors affecting MACE events

Factor	P value	Factor	P value	Factor	P value
Gender	.618	CHF	.387	Hb	.315
Frailty	.410	Syncope	.825	Creat	.897
Diabetes	.502	Prev radiation	.412	Pro bnp	.460
COPD	.671	Porcelain aorta	.867	Serum albumin	.460
BMI	.643	Nyha	.196	Serum protein	.573
Stroke	.357	MR	.344	Annulus diameter	.101
PAD	.671	AS grad	.333	Lv systolic pressure	.530
HTN	.671	PROSTHESIS TYPE	.942	LV ed	.202
CKD	.867	POST DILATION	.108	Aortic systolic pr.	.202
Prev MI	.163	STS SCORE	.574	Aortic diastolic prss.	.149
Prev PCI	.671	EUROSCORE2	.426	Mean gradient	.315
Prev CABG	.410			Prosthesis size	.573
Prev AVR	.570			Post nt pro bnp	.829
				Post trop	.635

DISCUSSION

In present study the results have been reported of post TAVI patients of followup upto one year. The interquartile range of age of patient undergoing impantation was 71-79 (25^{th}-75^{th}) with median age of 75. As per the latest US TVT regitry in 2018 the interquartile range of implantation was 75-86(25^{th}-75^{th}) with median age of 81. The mean STS score in our study was 5.5 +/-1.8, while that in the US TAVI registry it was 5.0% in 2018. TAVI has evolved from the patients with high risk to patients with low surgical risk which is evident from the declining mean STS score of US TAVI data every year. In the present study 89% were in intermediate to high risk for procedure while other had frialty or porcelain aorta. For low surgical risk still surgical valve remians the preferred option, which reflets the lesser acceptance of procedure in Indian population mainly due to financial constraints.

In India valves which are mainly available include the Corevalve, Evolute R, Edward sapien3 and the indigenous valves Myval and Hydravalve. In present study patients underwent implantation with Corevalve, Evolute R, Edward sapien 3 and Myval. The latest US and UK registries include the latest generation and better profile valves including Lotus, Symetis accurate, portico and direct flow medical.

Deaths due to calcific AS has been rising in india which was 4898 in 2017 . If we extrapolate data to Indian population nearly 2.5-3 lakh patients with AS will be elegible for TAVI. But currently TAVR is done at 30 centres across India while major load is handled by 7 centres, which is far below the number of cardaic cath labs across country.

In the present study majority underwent TAVI for degenerative tricuspid aortic valve while 8.7% had rheumatic aortic valve and 13% patients had bicuspid aortic valve

The principal finding in out study was no mortality upto 1 year followup. The mortality from any cause observed in FORWARD study with almost sismilar STS risk score(5.5+/-4.5) was 8.9% over 1 year followup, while that seen in US TAVI registry was 13.9 %.[47] The cause of cardiovascualr mortality as seen in the other studies has been mainly the heart failure. Other being sudden cardiac death, infective endocarditis, major stroke or major bleeding,

As per metanalysis including 28 TAVI studies overall 46.4% and 51.6% of deaths were related to noncardiovascular causes within and after the first 30 days, respectively. Within 30 days of TAVR, infection/ sepsis (18.5%), heart failure (14.7%), and multiorgan failure (13.2%) were the top 3 causes of death. Beyond 30 days, infection/sepsis (14.3%), heart failure (14.1%), and sudden death (10.8%) were the most common causes.[48] The avaerage age of impantation of valve was lower in the present study which could be an explaiantion of mortality difference compared to other studies.

Access site complications

Major access site complications needing surgical interventions were seen in 8.7% of patients in our study while one patient had limb ischemia after which patient had to undergo limb amputation. Major access complications were seen in 7.1% in FORWARD study with Evolute R self expanding valves.[47] Pol TAVI registry showed access site complications in 9.64% of patients .[49] It was seen that left side access and female sex were independent factors for all vascular complications. Despite evolution in device technology including smaller delivery sheath profiles still acess site complication is a major issue. Minimum diameter needed for TAVI has been recommended to be 5 mm, else the other access sites should be considered including transapical, dierct arotic, carotid artery, subclavian/axillary or inferior vena caval access. Caval access is reserved where no viable access site is present and aorta is accessed from vena caval route by creating an AV fistula.[50]

Recent data from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (STS/ACC TVT) Registry suggest that the frequency of overall vascular complications is declining over time. In a registry analysis of 26,414 patients comparing outcomes in patients who underwent TAVR between 2012 and 2013 to those who did so in 2014, the incidence of major bleeding, life-threatening or disabling bleeding and vascular complications declined from 5.5% to 4.2%, 6.4% to 4.3%, and 5.6% to 4.2%, respectively.[51] Vascular complications are significantly lower with newer generation TAVR devices that require smaller delivery sheaths (major vascular complications were reduced from 8% (22–24 Fr sheaths) to 1% (18–19 Fr sheaths). One factor which was found to be associated with increased risk was larger sheath to femoral artery ratio >=1.05.[52]

Heart failure hospitalisation.

In the present study we reported readmission for heart failure upto 17.3% at 1 year of followup. A single study by Nombela-Franco et al. (6) reported the incidence of readmission up to 1 year after TAVR and showed that TAVR was involved in 43.9% of all-cause readmissions. Among this 41.1% were for cardiac causes, mainly CHF (23.3%).[53] Another study by Eric Durand et al. showed that in the year following TAVR, about one-quarter of patients were readmitted for CHF.[54] The mortality rate was high and significantly higher in the group of patients readmitted for CHF and increased with the number of readmissions They found factors independently associated with CHF readmission were low aortic mean gradient before TAVR, post-procedural blood transfusion, severe persistent post-procedural pulmonary hypertension, and left atrial dilatation . Studies with newer generation valves including FORWARD study (Evolute R) showed HF readmission of 8%, while SOURCE 3 (Sapien 3) showed HF hospitalisation rate of 8.1% in one year.

Post implantation AR

In our study there was no patient with more than mild aortic regurgitation post TAVI. Paravalvular AR has been dubbed the “Achilles’ heel” of TAVI, being one the significant complications of the technique. Recent meta-analysis performed by Villablanca et al. which included 46 observational studies and 4 randomized controlled trials enrolling a total of 44,247 patients found an incidence of moderate or severe AR of 6.7% after TAVI compared to only 0.8% in patients treated with SAVR.[55] Moderate to severe PAR was observed in 1.6% after Sapien 3 implantation compared to 6.9% after Sapien XT, according to the meta-analysis performed by Ando et al.[56] . Another metaanalysis confirmed these findings, with a lower incidence of PAR with the Sapien 3 valve: 5.58% vs. 19.35%, OR: 0.27.[57] The improvement with the Evolut-R THV as compared to the previous CoreValve is less spectacular: the Swiss registry, using VARC-2 definitions, found no significant difference in PAR ≥ 2 between the two devices (8.5% vs. 10.6%).[58] However, the analysis of SE devices from the TVT registry found a significant reduction of moderate or severe PAR in favor of Evolut-R: 4.4% vs. 6.2%, $p < 0.001$.[59] The latest generation of EvolutPRO valve showed no moderate or severe regurgitation in the pilot study including 60 patients.[60] The majority of patients, 72.4%, showed absent or trace PAR. The meta-analysis by Athappan et al. found

three major predictors of PAR: (1) valve undersizing, (2) aortic valve calcification, and (3) implantation depth.[61] More than mild residual PAR after surgical valve replacement is associated with an almost double risk of mid-term mortality. A meta-analysis of 45 studies, including 12,296 patients, has found a HR of 2.27 for increased 1-year mortality in patients with moderate or severe PAR.[61] A more recent meta-analysis including 15,131 patients confirmed the negative impact on survival.[62] Mild residual PAR was also associated with a higher risk of 1-year mortality, with a HR of 1.83, but it was no longer significant after sensitivity analysis. Another multicentric study using VARC-2 definitions, including 1735 patients implanted with SE and BE THV, found no impact of mild PAR on mortality after a median follow-up of 21 ± 17 months.

Valve leaflet thrombosis

8.7% of patients in our study has raised gradients on followup evaluation which was found to be secondary to leftlet thrombosis as confirmed on CT scan. Valve thrombosis has been defined, according to Valve Academic Research Consortium 2 criteria as "any thrombus attached to or near an implanted. valve that occludes part of the blood flow path, interferes with valve function, or is sufficiently large to warrant treatment".[63] Transcatheter aortic valve thrombosis(TAVT) has an incidence ranging from 0.61% to 2.8%.[64,65] It can be classified, according to its timing, into acute (0–3 days after TAVI), subacute (3 days to 3 months after TAVI), late (3 months to 1 year after TAVI), and very late (>1 year after TAVI) [6]. In the study by Latib et al. on 4,266 patients undergoing TAVI, all cases of TAVT were detected within 2 years after valve implantation with a median time to thrombosis of 181 days.[64] Despite TAVT may occur without a specific underlying cause, several predisposing factors such as valve-in-valve procedures, obesity, use of a balloon-expandable valve, and a small prosthesis size (<23 mm) have been identified as independent predictor of TAVT. In our study both patients were non compliant to antiplatelet drugs. They were started on oral anticoagulation after which gradients subsequently decreased. Current AHA 2020 recommends Class 2a for aspirin life long, 2b for dual antiplatelet for 3-6 months and 2b for oral anticoagulation for 3 months.

Need for pacemaker impantation

In the present study post TAVI LBBB was seen in 4.3%, transient LBBB in 8.7%, while complete heart block was seen in 8.7% and transient CHB in 4.3%. 8.7% pateints had to undergo pacemaker implantation post procedure. New onset LBBB has been seen in 4-30% using balloon expandable Edward Sapien and Sapien XT valve and 18-65% using self expandable Medtronic Corevalve.[66] New onset LBBB after TAVI using Edwards Sapien 3 varies from 12-22%.[67] Around 17%(ranging incidence of 2-51%) of patients developed severe conduction disorders requiring PPI after first generation device. The first randomized trials with TAVI, the PARTNER 1-2 and the US CoreValve trial, reported PPI rates from 3.6% to 19.8%. PPI rate of the latest commonly used TAVI devices are Edwards Sapien3 11-14%, Medtronic Evolute R 15-22%, Lotus 28-37%, Symetis Acurate Neo 5-11%, Jena Valve 12-15% and Portrico 4.5-10%.[67-69] Patient related risk factors for PPI include male gender and preexisting conduction disorders such as RBBB, first degree heart block or left anterior hemiblock. In our study all patients had transient or persistent CHB for which PPI was done. Calcifications of the aortic annulus, LVOT and mitral annulus are also associated with PPI after TAVI. 2-3 times increased risk of conduction disorder requiring PPI is reported in self expandable Corevalve prosthesis compared to balloon expandable Edward sapien. Other procedural factors are intraop high grade AV block, more than 10% oversizing and lower implantation depth. For delayed high grade AV block >24 hours after TAVI, male gender, pre existing RBBB, new onset LBBB or RBBB after TAVI and prolonged QRS duration are independent risk factors reported. A large metanalysis showed that after PPI there was no increased risk of mortality after TAVI.[40] However a recent American registry showed a higher mortality rate after 1 year post PPI secondary to left ventricular dysfunction and heart failure dur to long term RV pacing.[70]

Stroke

Present study showed stroke rate of 13% which was quite high compared to other major studies. Rate of stroke has been reported to be about 3-6% after TAVI as per various studies. Highest rate of CVA is during valve positioning and deployment with second highest during balloon aortic valvuloplasty. In our study majority patients had stroke post valve implantation.[71] In addition studies suggest that upto 84% of patients

have silent ischemic embolic lesions spread across both hemispheres consistent with embolic showering events.[72] Some studies suggest that majority of lesions resolve by 3 month followup. Stroke is associated with 5-10 fold increased risk of short term mortality.[73,74] Risk of stroke in PARTNER 1 was over twice as high in the TAVI cohort as SAVR(5.5% vs 2.4%).In PARTENER 2a it was found to be 3.1% , which was lower than SAVR (5.4%). Data from TVT registry report stroke rate of 2.5% at 30 days and 4.1% at 1 year.[75] PARTNER cohort A study found that smaller AV area index was associated with increased risk of early neurological events. In addition studies have found that preexisting atrial fibrillation or new onset atrial fibrillation after TAVR was associated with 4 fold increased risk of in hospital or late strokes. From a procedural standpoint, balloon post dilation has been associated with increased risk. In similar cohort as the present study the one year stroke rate was found to be 3.4% in FORWARD study and 3.1% in SOURCE 3 study. Despite improvements in valve design, rates of neurological event tend to persist. Multiple devices have been developed which uses filteration or diversion system for cerebral protection. Some of the devices include EMbol X, Embrella embolic delector, Trigaurd, Sentinel cerebral protection system. The use of embolic devices has been studied in various small trials. Meta analysis including 16 studies did not show any benefit in rate of decrease in stroke.[76]

Valve in Valve

In the present study Valve in valve TAVR was done in 13% patients. One patient had severe patient prosthesis mismatch on followup and another patients had mdoerate mismatch. Patients with severe mismatch had hospital admission for heart failure, during which frame fracture was done after which gradients decreased to mild obstruction. Mohty et al. found that severe PPM was associated with decreased 5 and 10 year survival (74% and 40% respectively) significantly worse than patients with no or mild PPM (84% and 61% respectively).[77] The earliest database to evaluate VIV TAVR have been the VIVID and STS/TVT registries. Overall mortality at 30 days was 4.6% of 1168 patients undergoing VIV TAVR that were included in VIVID registry, 2.1% in 1150 patients in TVT registry, 0.7 % in the continued access patients of the Partner 2 VIV registry, 8% in a meta-analysis of 14 series published prior to 2015.[78,79]

Presence of a small surgical valve <=23 mm, and aortic stenosis, rather than regurgitation was associated with increased mortality in VIVID registry.[80] In a recent long term series by de Freitas Campos Guimaraes et al. with a median follow-up of 3 years after VIV TAVR, 25.9 % of patients had died (17.2% from cardiovascular causes).[81] In TVT registry, the rate of moderate to severe paravalvular leak was lower in VIV TAVR compared to TAVR in native valve (3.5% vs 6.6%), but mean gradients were higher (16 mm vs 9 mm). Rate of stroke was 1.7% at 30 days, new pacemaker 3.0%, both lower than patients in whom native valve TAVR was being performed. Over 30% of VIV procedures in STS TVT and VIVID registries resulted in severe residual gradients postoperatively. In a series of 20 patients with severe PPM, who underwent valve fracture there was no root rupture, coronary obstruction, or need for pacemaker.[82] Fifteen of 20 procedures were performed after placement of TAVR valve. In these cases, mean gradient decreased from 20.5 mmHg after ViV TAVR to 6.7 mmHg($p<0.001$) and EOA from 1.0 cm2 to 1.8 cm2 ($p <0.001$).

CONCLUSIONS

In patients with intermediate to high risk there was no mortality after transcatheter valve implantation at one year of followup.

No patient had moderate to severe paravalvular regurgitation on followup, though a few were found to have prosthetic valve leaflet thrombosis which improved with anticoagulation.

The mace events were quite high in the form of increased heart failure hospitalization and stroke rate at followup of one year.

Patient prosthesis mismatch is higher in patients with valve in valve implantation. Frame fracture was found to effectively decrease the stenosis severity.

Preexisting right bundle branch block was found to be associated with increased need for pacemaker implantation post TAVI. No other baseline or procedural factor was found to correlate with the final clinical outcome.

Only femoral access was used for valve implantation in the present study. Access site complications was seen in number of patients, while a few needed surgical repair for it.

LIMITATIONS

Sample size is small so results cannot be generalized to overall population.

All the patients couldnot be followed up due to time constraints for study completion which could affect the outcome data.

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APPENDIX

APPENDIX 1- PROFORMA **TAVI DATE-**

Patient initials AGE- GENDER- HOSPITAL NO.

Address- MOBILE NO.

STS RISK SCORE- EUROSCORE 2

BMI-

FRAILITY (GENERAL APPERANCE) YES NO

DM- YES NO

COPD YES NO

STROKE YES NO

PAD YES NO

HTN YES NO

PREVIOUS MI YES NO

PREVIOUS PCI YES NO

PREVIOUS CABG YES NO

PREVIOUS BAV YES NO

CHF YES NO

OTHER MAJOR COMORBIDITIES

PREVIOUS MEDIASTINAL RADIATION

PORCELAIN AORTA

NYHA CLASS

HEMOGLOBIN

CREATININE

NT PROBNP

TROP T

S. ALBUMIN

PREVIOUS TAVI/AVR

CURRENT CORONARY ANGIOGRAM

ECHO

EF

PAP

TRANSVALVULAR VELOCITY

TRANVALVULAR GRADIENT

AORTIC VALVE AREA

AORTIC REGURGITATION

MITRAL STENOSIS

MITRAL REGURGITATION

CT ANGIO

PERIMETER

ANNULUS DIAMETER

ANNULUS AREA

SINOTUBULAR JUNCTION

CORONARY HEIGHT

LVOT BULGE

DIAMETER OF CFA,EIA,CIA

OTHER VASCULAR ANOMALIES

ECG

PR INTERVAL

BUNDLE BRANCH BLOCK

AV BLOCK

ARRHYTHMIA

PROCEDURAL DETAILS

PROCEDURAL TIME

ACCESS CLOSURE DEVICE

PRE BALLOON DILATION

PROSTHESIS SIZE

USE OF CONTRAST

POST PROCEDURE GRADIENT

POST PROCEDURE AR

POST BALLOON DILATION

ACCESS COMPLICATIONS

PROCEDURAL COMPLICATIONS

CONCOMITANT PROCEDURES

HEMODYNAMIC DATA			
	LV	AORTA	GARDIENT
PRE			
POST			

POST PROCEDURE

TROP- DAY 1

PRO BNP DAY 1

LENGTH OF HOSPITAL STAY

SIGNS OR SYMPTOMS YES NO

STROKE YES NO

MI YES NO

RENAL FAILURE YES NO

NEED FOR PPI YES NO

NEED FOR PROLONGED VENTILAOTRY SUPP(>24 HRS) OR NEED FOR REINTUBATION

. YES NO

NEED FOR BLOOD TRANSFUSION YES NO

ATRIAL FIBRILLATION YES NO

EMERGENCY SURGERY

1 MONTH FOLLOWUP

NYHA CLASS

LV EF

AORTIC VALVE GRADIENT , AREA AND AR,

ACS	YES	NO
VALVE THROMBOSIS	YES	NO
CVA	YES	NO

ECG- AV BLOCK/ BUNDLE BRANCH BLOCK / ATIRAL FIB

COMPLIANT TO ANTIPLATELETTE/ANTITHROMBOTIC	YES	NO
HOSPITAL ADMISSION FOR HF	YES	NO
MORALITY	YES	NO

1YEAR FOLLOWUP

NYHA CLASS

LV EF

AORTIC VALVE GRADIENT , AREA AND AR,

ACS	YES	NO
VALVE THROMBOSIS	YES	NO
CVA	YES	NO

ECG- AV BLOCK/ BUNDLE BRANCH BLOCK / ATIRAL FIB

COMPLIANT TO ANTIPLATELETTE/ANTITHROMBOTIC	YES	NO
HOSPITAL ADMISSION FOR HF	YES	NO
MORALITY	YES	NO

APPENDIX 2- IEC APPROVAL

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/1371/APRIL-2019 19.07.2019

Dr. Ankur Agarwal
Resident
Department of Cardiology
SCTIMST, Thiruvananthapuram

Dear Dr. Ankur Agarwal,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "EARLY AND ONE YEAR OUTCOMES AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION (IEC/1371)" on 12th April, 2019.

The following documents were reviewed:

Original submission

1. *Covenng letter addressed to the Chairperson, IEC, SCTIMST dated 15.03.2019 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Patient Information Sheet and Informed Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co- Principal Investigators*

Revised submission

1. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 08.07.2019 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Patient Information Sheet and Informed Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co- Principal Investigators*

Page 1 of 2

The following members of the Ethics Committee were present at the meeting held on 12th April, 2019 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. Rema M. N	MD	Female	Basic Medical Scientist	No
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
5.	Dr. Harikrishna Varma PR	Ph.D(Materials Science)	Male	Medical Technology	Yes
6.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
7.	Dr. S S Giri Sankar	LL.M. Ph.D.	Male	Legal Expert	No
8.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
9.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
10.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
11.	Dr. Anand Kumar A	MD, DM	Male	Clinician	No
12.	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

APPENDIX 3- CONSENT FORM

STUDY CONSENT FORM

TITLE OF THE STUDY: EARLY AND 1 YEAR OUTCOMES AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION.
Study number: All patients undergoing TAVI at SCTIMST will be included in study

Participant's name: Date of Birth / Age (in years):
I_____ _____,
son/daughter of _____

(Please tick boxes).

[ ] Declare that I have read the above information provided to me regarding the study: "Early and 1 year outcomes after transcatheter aortic valve implantation." and 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 may 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 may not be revealed in any information released to third parties or published.

[ ] 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:	Date:

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.

_____ _____

Name and Signature of Person Obtaining Consent
Dr. Ankur Agarwal
Senior resident
Dept. of Cardiology SCTIMST

For any technical clarifications, please contact Dr. Mala Ramanathan, Member Secretary, IEC, SCTIMST and Additional Professor, AMCHSS, SCTIMST (Email: iec.mem.sec@sctimst.ac.in, Phone no. 0471-2524234)

APPENDIX 4- PATIENT INFORMATION SHEET

SREE CHITRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

PATIENT INFORMATION SHEET

TITLE: EARLY AND 1 YEAR OUTCOMES AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION

Name of Investigators:
DR ANKUR AGARWAL, DR BIJULAL S., DR AJIT KUMAR VK

Dear Patient/Parent

We welcome you and thank you for your interest in this research project titled "EARLY AND 1 YEAR OUTCOMES AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION". Before your participate in this study, it is important for you to understand why this research is being carried out. This form will provide you all the relevant details of this research. It will explain the nature, the purpose, the benefits, the risks, the discomforts, the precautions and the information about how this project will be carried out. It is important that you read and understand the contents of the form carefully. This form may contain certain scientific terms and hence, if you have any doubts or if you want more information, you are free to ask the study personnel or the contact person mentioned below before you give your consent and also at any time during the entire course of the project.

Aortic valve is the valve situated between the left ventricle(heart major chamber) and aorta(major blood vessel arising from left ventricle). Function of the valve is to prevent blood from flowing back into the ventricle and maintain flow in one direction. Valve can be damaged in various diseases which can result in aortic stenosis-AS (narrowing) or aortic regurgitation- AR (leaking). Severe aortic stenosis or regurgitation require valve replacement. Established treatment for AS or AR is surgical aortic valve replacement. Risk of death associated with surgical AVR is 1-3%. But in those with underlying diseases risk of surgical AVR is higher, and in these patients Transcatheter Aortic Valve Implant/ Replacement (TAVI/TAVR) is the preferred treatment strategy.

Advantages of TAVR over surgery
1-No need of opening of chest
2-No need of cardio pulmonary bypass
3- No need for prolonged ventilation
4- Less bleeding
5- Quick recovery
6- Early ambulation
7- Early discharge from hospital

Even though TAVR safer compared to surgery(established in large clinical trial ie PARTNER trial), it also carries risk which include

0

1-Bleeding from access site- 2-5%
2- Stroke- 2-3%
3- Complete heart block with low heart rate needing permanent pacemaker implantation- 5%
4- Cardiac perforation and tamponade needing urgent surgery- 1-2%
5- Vessel trauma needing surgery
6- Death 1-4%
7- Occlusion of coronary artery and heart attack- 1%
8-Severe leak from newly implanted valve -3-5%
9- Infection

Procedure steps
1- Patient will be given general anaesthesia and given mechanical ventilation
2- Suitable vascular access will be obtained- Require 2-3 vascular access, and a plastic tube (introducer) is inserted into an artery in your groin (femoral artery).
3- Temporary pacing support will be obtained
4- Native Aortic valve will be dilated with suitable sized balloon
5- New valve will be implanted at location of native aortic valve and function will be assessed by echocardiogram and angiogram
6- Access site will be closed and patient will be shifted to ICU for 48 hr observation

What does the present study involve?

The records of the previous operation that you have undergone will be collected from the hospital database. You will be contacted by phone/ by mail to visit the hospital on a particular day. You will usually come in to hospital on the day of appointment. A specialist doctor will explain the proposed study design to you and ask you to sign the consent form to confirm that you understand the procedure and agree to go ahead with it. Please ask any questions you want.

Following enrolment into the study, you will undergo the following tests- usually done as part of routine follow up evaluation:

- Functional status- History
- Electrocardiogram
- Echocardiogram
- Any other test deemed necessary as part of evaluation

How long does it take?

The hospital visit will be a routine consultation, and the tests done will be part of routine follow up. This may take upto 2-3 hours. Please be prepared to be in the hospital OPD during that time.

WHAT ARE THE RESPONSIBILITIES OF PARTICIPANTS?

Your decision to participate in this study is voluntary, your own personal choice. You may choose not to continue at any time, for any reason, without notice.

WHAT ARE THE EXPECTED RISKS FOR THE PARTICIPANTS?

The study involves collection of previous data from case records, and a follow up evaluation to assess the functional status and outcome of prior surgery. There will be no risks for the participants because of participation in the study. They will be managed according to the hospital protocol. No specific intervention will be done.

WHAT ARE THE EXPECTED BENEFITS OF THE RESEARCH TO THE PARTICIPANTS?

The participants are evaluated in detail for any cardiac cause for functional impairment. A follow up examination and evaluation may be helpful in identification of any risk factors for poor outcomes or functional deterioration. It may be helpful in detecting patients who require early intervention or addition of medical therapy . The data derived from the study may be helpful in planning appropriate timing and surgical strategies for patients with similar conditions in the future.

WILL PARTICIPANTS BE COMPENSATED FOR PARTICIPATION IN THIS TRIAL?

You will not be paid for participation in the study.

WILL MY PARTICIPATION IN THIS STUDY BE KEPT CONFIDENTIAL?

All records of your study will be kept confidential. Your identity will not be revealed in any publication or release of results. Study records will be kept indefinitely for analysis and follow-up.

CAN I WITHDRAW FROM THE STUDY AT ANY TIME DURING THE STUDY PERIOD?

Yes, you can. Your decision will not affect your regular medical care.

IF THERE ARE ANY NEW FINDINGS / INFORMATION, WOULD I BE INFORMED?

Yes.

WHAT HAPPENS IN CASE OF A STUDY RELATED INJURY?

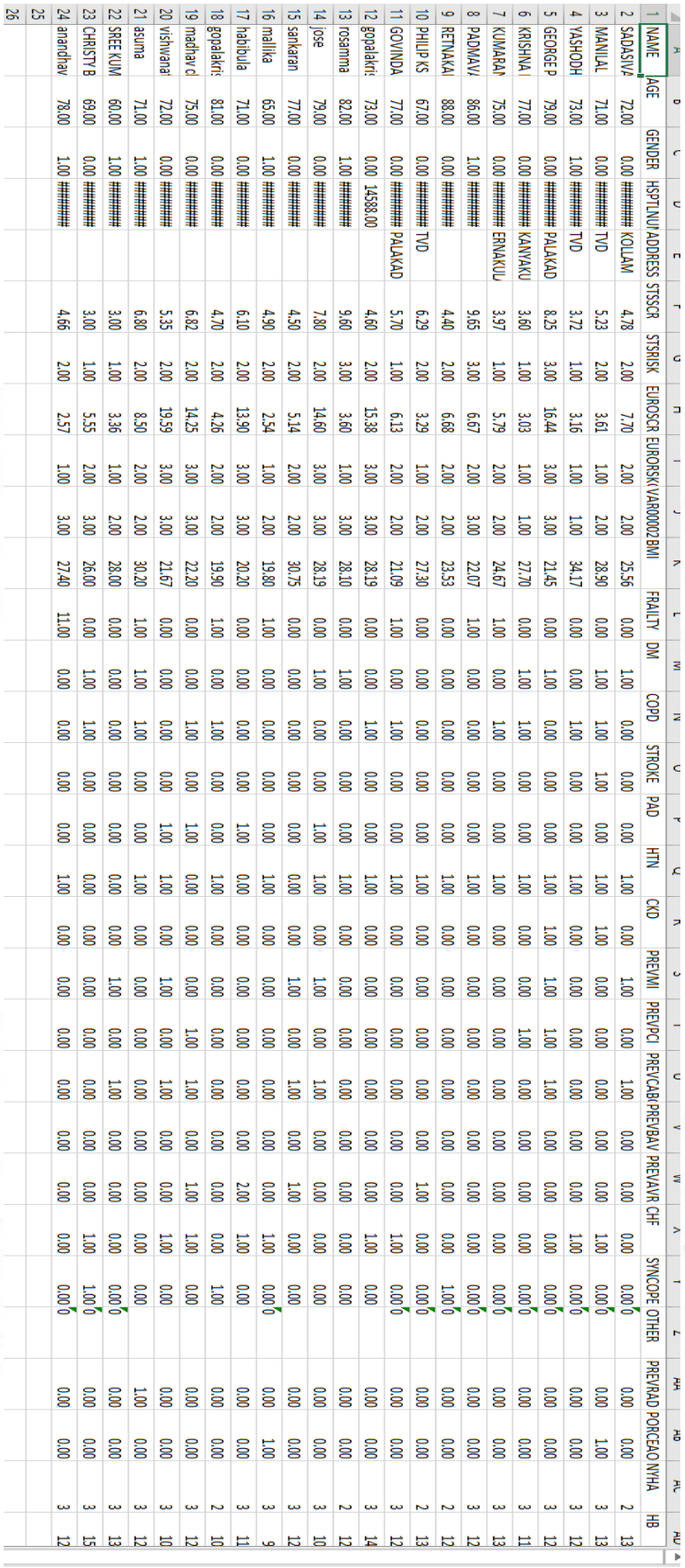
There will be no study related injury.

IS THERE ANY ALTERNATIVE TO THE TREATMENT MENTIONED?

Not applicable.

If you have any further questions, please ask: Dr. Ankur Agarwal (Principal investigator), Senior Resident, Department of Cardiology (Email: ankuragarwal@sctimst.ac.in Ph No: 9718240933)
For any technical clarifications, please contact Dr. Mala Ramanathan, Member Secretary, IEC, SCTIMST and Additional Professor, AMCHSS, SCTIMST (Email: iec.mem.sec@sctimst.ac.in, Phone no. 0471-2524234)

APPENDIX 5- MASTER CHART



NAME	AGE	GENDER	HSPTLNUM	ADDRESS	STSSCR	STSRISK	EUROSCR	EUROSK(VAR00002	BMI	FRAILTY	DM	COPD	STROKE	PAD	HTN	CKD	PREVMI	PREVPCI	PREVCABG	PREVBAV	PREVAVR	CHF	SYNCOPE	OTHER	PREVRAD	PORCEAO	NYHA	HB
SADASIVA	72.00	0.00	########	KOLLAM	4.78	2.00	7.70	2.00	25.56	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2	13
MANILAL	71.00	0.00	########	TVD	5.23	2.00	3.61	1.00	28.90	0.00	1.00	1.00	0.00	0.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	3	13
YASHODH	73.00	1.00	########	TVD	3.72	1.00	3.16	1.00	34.17	0.00	1.00	1.00	0.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	3	12
GEORGE P	79.00	0.00	########	PALAKAD	8.25	3.00	16.44	3.00	21.45	0.00	1.00	0.00	0.00	0.00	1.00	1.00	1.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3	12
KRISHNA I	77.00	0.00	########	KANYAKU	3.60	1.00	3.03	1.00	27.70	0.00	1.00	1.00	0.00	0.00	1.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3	11
KUMARAN	75.00	0.00	########	ERNAKULA	3.97	1.00	5.79	2.00	24.67	1.00	0.00	1.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3	13
PADMAVA	86.00	1.00	########		9.65	3.00	6.67	2.00	22.07	1.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3	12
RETNAKA	88.00	0.00	########		4.40	2.00	6.68	2.00	23.53	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	2	12
PHILIP KS	67.00	0.00	########	TVD	6.29	2.00	3.29	1.00	27.30	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	2	13
GOVINDA	77.00	0.00	########	PALAKAD	5.70	1.00	6.13	2.00	21.09	1.00	0.00	1.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3	12
gopalakris	73.00	0.00	14588.00		4.60	2.00	15.38	3.00	28.19	0.00	0.00	1.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	3	14
rosamma	82.00	1.00	########		9.60	3.00	3.60	1.00	28.10	0.00	1.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2	12
jose	79.00	0.00	########		7.80	2.00	14.60	3.00	28.19	0.00	1.00	0.00	0.00	1.00	1.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3	10
sankaran	77.00	0.00	########		4.50	2.00	5.14	2.00	30.75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	3	12
mallika	65.00	1.00	########		4.90	2.00	2.54	1.00	19.80	1.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	1.00	3	9
habibula	71.00	0.00	########		6.10	2.00	13.90	3.00	20.20	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	2.00	1.00	0.00	0.00	0.00	0.00	3	11
gopalakris	81.00	0.00	########		4.70	2.00	4.26	2.00	19.90	1.00	0.00	1.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	2	10
madhav cl	75.00	0.00	########		6.82	2.00	14.25	3.00	22.20	0.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	3	12
vishwanat	72.00	0.00	########		5.35	2.00	19.59	3.00	21.67	0.00	0.00	0.00	0.00	1.00	1.00	0.00	1.00	0.00	1.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	3	10
asuma	71.00	1.00	########		6.80	2.00	8.50	2.00	30.20	1.00	1.00	1.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	3	12
SREE KUM	60.00	1.00	########		3.00	1.00	3.36	1.00	28.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3	13
CHRISTY B	69.00	0.00	########		3.00	1.00	5.55	2.00	26.00	0.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	1.00	0.00	0.00	0.00	3	15
anandhav	78.00	1.00	########		4.66	2.00	2.57	1.00	27.40	11.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3	12

	CREAT	PROBNP	TROP	SALB	CORONAF	PROTEIN	EF	EF1	PAP	ETIOLOGY	CUSP	ASGRAD	ASSEV	AR	MS	MR	PERIMETE	ANNULDI	ANNAREA	SINUSDIA	STJ	ASCAORT	RTCORHT	LTCOROH	RCIA	LCIA	RTEIA	LTEIA	RFA	LFA
1	CREAT	PROBNP	TROP	SALB	CORONAF	PROTEIN	EF	EF1	PAP	ETIOLOGY	CUSP	ASGRAD	ASSEV	AR	MS	MR	PERIMETE	ANNULDI	ANNAREA	SINUSDIA	STJ	ASCAORT	RTCORHT	LTCOROH	RCIA	LCIA	RTEIA	LTEIA	RFA	LFA
2	0.90	342.00	#NULL!	4.50	5.00	8.10	45.00	1.00	1.00	1	3.00	41.00	3	1.00	0.00	2.00	65.60	23.00	3.19	26.60	24.30	23.30	15.00	12.50	10.50	8.80	7.90	8.00	8.80	8
3	1.53	3000.00	#NULL!	4.90	0.00	8.00	76.00	0.00	0.00	1	3.00	50.00	3	3.00	1.00	1.00	67.50	23.10	3.47	29.10	24.80	31.10	9.80	12.60	9.80	10.80	8.10	8.30	8.30	8
4	0.81	2000.00	#NULL!	3.90	0.00	8.00	86.00	0.00	1.00	1	3.00	60.00	4	1.00	0.00	1.00	72.50	24.00	3.98	30.00	27.70	28.00	18.00	10.00	13.00	12.60	9.00	9.00	11.10	11
5	1.55	5000.00	190.00	4.00	4.00	8.30	33.00	2.00	1.00	3	2.00	58.00	3	1.00	0.00	3.00	78.70	26.40	4.54	33.60	31.60	36.80	16.80	20.30	10.50	8.80	8.00	8.00	8.80	7
6	0.87	390.00	16.00	3.70	1.00	6.90	63.00	0.00	0.00	1	3.00	42.00	3	2.00	0.00	1.00	76.00	27.20	4.39	35.40	33.30	40.00	14.80	16.20	11.50	10.00	7.40	7.50	6.40	7
7	1.07	5540.00	#NULL!	3.60	0.00	8.30	50.00	1.00	1.00	1	3.00	45.00	3	1.00	0.00	3.00	66.80	23.30	3.43	28.30	23.60	29.90	13.90	14.00	9.15	9.35	6.69	6.18	9.14	7
8	1.18	8410.00	230.00	3.60	0.00	7.60	48.00	1.00	1.00	1	3.00	43.00	3	3.00	0.00	3.00	66.40	22.70	3.34	35.20	33.50	39.40	12.00	14.60	7.85	8.20	5.60	6.50	6.28	6
9	1.14	8810.00	#NULL!	3.50	0.00	6.60	45.00	1.00	0.00	1	3.00	85.00	4	2.00	0.00	3.00	77.30	28.20	4.48	27.70	24.70	31.50	12.10	12.50	10.40	8.90	9.40	8.60	9.80	8
10	1.32	557.00	#NULL!	4.60	0.00	8.30	76.00	0.00	1.00	1	3.00	25.00	2	4.00	0.00	2.00	60.00	20.10	2.68	34.00	25.60	38.00	7.38	9.81	10.50	11.10	7.54	8.08	9.27	8
11	0.95	5000.00	#NULL!	3.10	0.00	5.80	57.00	0.00	3.00	1	3.00	74.00	4	3.00	0.00	2.00	86.00	23.90	3.75	36.00	29.60	37.00	19.20	17.20	10.00	9.00	8.00	8.80	9.30	8
12	1.37	2870.00	#NULL!	2.20	0.00	5.20	45.00	1.00	2.00	1	3.00	46.00	3	3.00	0.00	3.00	65.00	25.00	3.80	29.00	27.00	40.00	24.00	11.00	10.00	9.80	8.00	8.20	8.50	8
13	0.90	3500.00	#NULL!	3.60	0.00	7.50	59.00	0.00	0.00	3	2.00	50.00	3	2.00	0.00	0.00	63.30	25.00	2.57	27.00	25.60	28.70	11.10	9.69	8.76	8.95	6.54	6.36	8.10	6
14	1.40	3200.00	#NULL!	3.10	5.00	6.20	50.00	1.00	1.00	1	3.00	46.00	3	1.00	0.00	2.00	72.00	19.60	3.00	30.00	33.00	32.00	13.00	12.00	8.60	8.50	8.00	8.00	8.00	7
15	0.99	5200.00	#NULL!	3.90	5.00	6.90	40.00	2.00	1.00	1	3.00	40.00	3	3.00	0.00	2.00	39.00	27.00	3.40	36.00	32.00	40.00	11.00	12.00	11.50	11.60	8.50	8.50	10.00	9
16	1.02	11400.00	#NULL!	4.60	1.00	8.20	66.00	0.00	3.00	3	2.00	41.00	3	4.00	0.00	3.00	77.00	29.00	3.80	38.00	35.00	40.00	12.00	11.00	9.00	8.50	6.50	6.70	7.00	7
17	1.36	3050.00	14.00	3.60	0.00	7.10	76.00	0.00	3.00	2	3.00	76.00	4	2.00	1.00	0.00	71.00	22.70	3.88	31.00	26.50	31.00	18.00	13.00	9.00	9.00	7.00	7.00	7.00	6
18	1.11	1100.00	#NULL!	3.90	0.00	8.20	64.00	0.00	1.00	1	3.00	64.00	4	1.00	0.00	2.00	65.00	29.00	4.00	36.00	34.00	37.00	20.00	18.00	11.00	10.00	7.60	7.10	8.70	8
19	1.08	1070.00	#NULL!	4.80	2.00	7.00	63.00	0.00	1.00	1	3.00	27.00	3	4.00	0.00	0.00	58.00	18.00	3.54	40.00	38.40	42.00	18.30	20.90	10.80	11.50	6.40	6.30	6.70	6
20	1.26	20000.00	2600.00	3.80	5.00	6.50	43.00	1.00	0.00	1	3.00	76.00	4	2.00	0.00	2.00	69.00	26.00	3.63	38.00	35.00	45.00	18.00	18.50	6.30	6.20	5.20	5.10	5.60	6
21	0.54	500.00	#NULL!	4.10	0.00	7.70	73.00	0.00	0.00	1	3.00	48.00	3	0.00	0.00	2.00	70.00	19.80	3.80	27.00	23.00	28.00	12.00	12.00	10.00	10.80	8.50	8.00	8.00	8
22	0.81	1300.00	16.00	4.30	4.00	7.90	69.00	0.00	0.00	1	3.00	0.00	0	4.00	0.00	2.00	78.00	26.00	4.01	33.00	30.00	33.00	13.00	15.00	9.80	9.70	8.00	8.00	8.20	8
23	1.44	6640.00	20.00	3.90	0.00	8.10	31.00	3.00	2.00	2	3.00	16.00	3	2.00	0.00	3.00	69.00	23.80	4.36	33.60	27.30	34.00	18.40	13.00	8.20	8.40	5.60	5.20	6.00	6
24	1.07	481.00	10.00	4.30	0.00	7.70	63.00	0.00	0.00	1	3.00	42.00	3	3.00	0.00	1.00	70.00	21.20	3.41	19.00	24.20	29.00	14.00	11.00	9.20	9.30	7.20	7.20	8.10	8
25																														

1	PRINT	PRPROLOI	BBB	ARRYTHM	CATHLVSF	CATHLVEF	CATHAOS	CATHAOD	CATHGRA	ECHOAR	CATHAR	PREDIALA	POSTDILA	PROSTHES	PROSTHES	IZEPROS	POSTGRAI	POSTAR	VAR00001	HEARTBL	ACCESSCL	ACCESSSI	OTHERCO	CONCPRCI	POSTTROI	POSTBNP	LENGTHH	SYMPT	POSTSTRC	POSTN
2	140.00	0	0.00	0.00	148.00	16.00	100.00	50.00	48.00	1.00	0.00	1.00	0.00	2	3	26.00	0.00	1.00	0.00	0.00	0.00	0	0	0	10.00	320.00	8.00	0.00	0.00	0
3	160.00	0	0.00	0.00	180.00	19.00	132.00	48.00	50.00	3.00	2.00	0.00	0.00	2	3	26.00	1.00	1.00	0.00	1.00	0.00	0	0	0	84.00	1150.00	7.00	0.00	0.00	0
4	160.00	0	0.00	0.00	170.00	18.00	110.00	60.00	60.00	1.00	2.00	1.00	0.00	2	3	21.00	0.00	2.00	0.00	0.00	1.00	HEMATON	EXTRAPEF	0	10.00	278.00	9.00	0.00	0.00	0
5	130.00	0	0.00	0.00	165.00	20.00	125.00	42.00	55.00	1.00	0.00	1.00	0.00	2	3	29.00	1.00	0.00	0.00	0.00	0.00	0	HYPOTEN	0	110.00	2340.00	13.00	0.00	2.00	0
6	130.00	0	0.00	0.00	190.00	18.00	142.00	57.00	48.00	2.00	2.00	1.00	1.00	1	2	23.00	0.00	1.00	0.00	0.00	0.00	0	0	0	10.00	329.00	7.00	0.00	0.00	0
7	130.00	0	0.00	0.00	180.00	18.00	120.00	60.00	46.00	1.00	0.00	1.00	0.00	1	2	23.00	1.00	0.00	0.00	0.00	1.00	RIGHT EIA	0	2	68.00	4810.00	16.00	0.00	0.00	0
8	160.00	0	1.00	0.00	180.00	25.00	164.00	40.00	16.00	3.00	3.00	1.00	1.00	2	3	26.00	0.00	1.00	0.00	0.00	0.00	0	0	0	230.00	4090.00	9.00	0.00	0.00	0
9	170.00	0	0.00	0.00	190.00	10.00	120.00	70.00	70.00	2.00	0.00	1.00	0.00	2	3	29.00	0.00	0.00	0.00	3.00	0.00	0	0	0	38.00	2800.00	6.00	0.00	0.00	0
10	130.00	0	3.00	0.00	150.00	20.00	98.00	52.00	22.00	4.00	4.00	1.00	0.00	2	3	23.00	0.00	1.00	0.00	0.00	0.00	0	0	0	10.00	310.00	7.00	0.00	0.00	0
11	220.00	0	2.00	0.00	242.00	24.00	103.00	36.00	139.00	3.00	2.00	1.00	1.00	1	2	26.00	0.00	2.00	1.00	4.00	0.00	0	0	1	23.00	4150.00	8.00	0.00	0.00	0
12	#NULL!		3.00	1.00	180.00	15.00	110.00	60.00	70.00	3.00	2.00	1.00	0.00	2	3	23.00	0.00	1.00	0.00	0.00	1.00	LEFTEIAD	0	0	13.00	1100.00	9.00	0.00	0.00	0
13	240.00	1	1.00	0.00	144.00	12.00	100.00	60.00	44.00	2.00	0.00	1.00	0.00	1	1	23.00	0.00	1.00	0.00	0.00	0.00	0	0	0	0.00	1290.00	7.00	0.00	0.00	0
14	240.00	1	1.00	0.00	160.00	20.00	112.00	48.00	44.00	1.00	0.00	1.00	1.00	1	2	21.00	0.00	0.00	0.00	0.00	1.00	LEFTPOPL	0	0	0.00	2300.00	9.00	0.00	0.00	0
15	180.00	0	0.00	0.00	135.00	30.00	100.00	30.00	30.00	3.00	3.00	1.00	0.00	1	1	26.00	1.00	0.00	0.00	3.00	0.00		0	0	0.00	1300.00	10.00	0.00	0.00	0
16	190.00	0	2.00	0.00	145.00	25.00	140.00	30.00	5.00	4.00	4.00	1.00	0.00	2	3	34.00	0.00	1.00	1.00	4.00	0.00		0	1	67.00	3180.00	12.00	0.00	0.00	0
17	#NULL!	0	0.00	1.00	200.00	18.00	130.00	40.00	70.00	2.00	2.00	1.00	0.00	1	2	23.00	0.00	1.00	0.00	0.00	0.00		0	0	0.00	2900.00	6.00	0.00	0.00	0
18	180.00	0	0.00	0.00	175.00	18.00	90.00	30.00	85.00	1.00	0.00	1.00	1.00	2	3	29.00	0.00	2.00	0.00	0.00	1.00	PSEUDOA	0	0	0.00	900.00	5.00	0.00	2.00	0
19	120.00	0	0.00	0.00	180.00	20.00	160.00	30.00	20.00	4.00	4.00	0.00	0.00	2	3	23.00	0.00	1.00	0.00	0.00	0.00		0	0	0.00	900.00	5.00	0.00	0.00	0
20	180.00	0	0.00	0.00	200.00	48.00	100.00	64.00	100.00	2.00	3.00	1.00	1.00	2	3	29.00	0.00	2.00	0.00	0.00	0.00	0		0	0.00	8000.00	5.00	0.00	1.00	0
21	180.00	0	2.00	0.00	170.00	18.00	120.00	70.00	50.00	0.00	0.00	1.00	0.00	2	3	23.00	0.00	0.00	1.00	5.00	0.00	0	0	0	0.00	500.00	5.00	0.00	0.00	0
22	220.00	1	1.00	0.00	120.00	15.00	120.00	50.00	0.00	4.00	4.00	0.00	0.00	2	3	29.00	0.00	0.00	0.00	0.00	0	0	0	0	0.00	900.00	6.00	0.00	0.00	0
23	#NULL!		1.00	1.00	130.00	6.00	110.00	70.00	20.00	2.00	0.00	0.00	0.00	2	3	29.00	0.00	1.00	0.00	0.00	1.00	post wall	0	2	10.00	3500.00	5.00	0.00	0.00	0
24	180.00	0	0.00	0.00	160.00	18.00	115.00	45.00	40.00	3.00	2.00	0.00	0.00	2	3	26.00	0.00	2.00	0.00	0.00	0.00	0	0	0	10.00	400.00	5.00	0.00	0.00	0
25																														

1	POSTMI	POSTRENA	POSTHB	VENTILAT	BLOODTRA	AFIB	EMERGSU	mace0	FRSTMON	FRSTMON	FRSTMON	FRSTMON	FRSTMON	FRSTMON	FRSTMON	firstmonti	FRSTMON	FRSTMON	FRSTMON	FRSTMON	FRSTMON	mace1	ONEYRNY	ONEYREF	ONERPV	ONERPV	ONERPV	ONERAC	ONERCV	ONERPV	ONERAR	ONEYR
2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	59.00	0.00	0.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	1.00	58.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0
3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.00	60.00	15.00	1.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	2.00	60.00	29.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0
4	0.00	1.00	0.00	0.00	1.00	0.00	0.00	0.00	1.00	73.00	0.00	1.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	2.00	60.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1
5	0.00	0.00	0.00	1.00	0.00	0.00	1.00	0.00	1.00	65.00	0.00	1.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	1.00	69.00	9.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0
6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.00	70.00	0.00	1.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	2.00	70.00	10.00	2.00	0.00	0.00	0.00	0.00	0.00	0.00	0
7	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	2.00	65.00	7.00	0.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	2.00	68.00	8.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0
8	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.00	55.00	0.00	0.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	2.00	56.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0
9	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	50.00	5.00	0.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	1.00	50.00	5.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0
10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	70.00	10.00	1.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	1.00	74.00	15.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0
11	0.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	60.00	0.00	2.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	0.00	0.00	1.00	65.00	0.00	2.00	0.00	0.00	0.00	0.00	0.00	0.00	0
12	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	3.00	54.00	45.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	1.00	1.00	0.00	2.00	50.00	26.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0
13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	70.00	0.00	0.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	1.00	80.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0
14	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	2.00	59.00	8.00	0.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	2.00	58.00	8.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.00	45.00	15.00	0.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	3.00	46.00	37.00	0.00	0.00	0.00	0.00	0.00	1.00	2.00	0
16	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	1.00	55.00	6.00	1.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	1.00	54.00	7.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0
17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	60.00	14.00	1.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	2.00	65.00	15.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0
18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	1.00	30.00	0.00	2.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	2.00	32.00	0.00	2.00	0.00	0.00	0.00	0.00	0.00	0.00	0
19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	60.00	0.00	0.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	1.00	63.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0
20	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	2.00	45.00	12.00	2.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	0.00	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NUL
21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	62.00	16.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NUL
22	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	70.00	0.00	0.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	0.00	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NUL
23	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.00	38.00	0.00	1.00	0.00	0.00	#NULL!	0.00	0.00	0.00	0.00	1.00	0.00	0.00	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NUL
24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NUL
25																																

	ONEYRNY	ONEYREF	ONEYRPV	ONEYRPV	ONEYRAC	ONEYRCV	ONEYRPV	ONEYRAR	ONEYRHF	ONEYRDR	ONEYEAR	ONEYRMC	mace12	duration	macenum	macebasa	maceone	maceone	TOTALMA	CUMULAT	survival	macewith	chb
2	1.00	58.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
3	2.00	60.00	29.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
4	2.00	60.00	0.00	1.00	0.00	0.00	0.00	0.00	1.00	1.00	0	0.00	1.00	12.00	1.00	0.00	0.00	1.00	1.00	1.00	6.00	1.00	0.00
5	1.00	69.00	9.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	1.00	1.00	0.00	0.00	1.00	1.00	0.00	1.00	0.00
6	2.00	70.00	10.00	2.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
7	2.00	68.00	8.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
8	2.00	56.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
9	1.00	50.00	5.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	00	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
10	1.00	74.00	15.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
11	1.00	65.00	0.00	2.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	1.00	1.00	0.00	0.00	1.00	1.00	0.00	0.00	1.00
12	2.00	50.00	26.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	1.00	0.00	1.00	0.00	1.00	1.00	1.00	1.00	0.00
13	1.00	80.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
14	2.00	58.00	8.00	0.00	0.00	0.00	0.00	0.00	1.00	1.00	LEFTFOOT	0.00	1.00	12.00	1.00	0.00	0.00	1.00	1.00	1.00	6.00	1.00	0.00
15	3.00	46.00	37.00	0.00	0.00	0.00	1.00	2.00	0.00	0.00	6.4PAUSE	0.00	2.00	12.00	1.00	0.00	0.00	2.00	1.00	1.00	6.00	1.00	0.00
16	1.00	54.00	7.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	1.00	1.00	0.00	0.00	1.00	1.00	0.00	0.00	1.00
17	2.00	65.00	15.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
18	2.00	32.00	0.00	2.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	1.00	0.00	0.00	1.00	1.00	0.00	1.00	0.00
19	1.00	63.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0	0.00	0.00	12.00	0.00	0.00	0.00	0.00	0.00	0.00	12.00	0.00	0.00
20	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!		#NULL!	#NULL!	#NULL!	#NULL!	1.00	0.00	#NULL!	#NULL!	1.00	0.00	1.00	#NULL!
21	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!		#NULL!	#NULL!	#NULL!	#NULL!	0.00	0.00	#NULL!	#NULL!	0.00	12.00	0.00	#NULL!
22	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!		#NULL!	#NULL!	#NULL!	#NULL!	0.00	0.00	#NULL!	#NULL!	0.00	12.00	0.00	#NULL!
23	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!		#NULL!	#NULL!	#NULL!	#NULL!	0.00	0.00	#NULL!	#NULL!	0.00	12.00	0.00	#NULL!
24	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!	#NULL!		#NULL!	#NULL!	#NULL!	#NULL!	0.00	#NULL!	#NULL!	#NULL!	0.00	12.00	0.00	#NULL!
25																							
26																							

APPENDIX 6- PLAGIARISM REPORT

Plagiarism Checker X - Report

Originality Assessment

Overall Similarity: **11%**

Date: Jan 29, 2021

Statistics: 1160 words Plagiarized / 10118 Total words