ECRONICON OPEN ACCESS

EC CARDIOLOGY
Mini Review

Coeval Trends in Aortic Stenosis: The Transformation to Transcather Gambit

Radhakrishnan Pradeep Kumar[1]*, Gayathri Ananyajyothi Ambat[2], Roshini Ambat[3], Nihas Nazer[4] and YA Nazer[4]

[1]Professor, Chief Division of Cardiothoracic and Vascular Surgery, GIMSR, GITAM University, Programme Coordinator TAH and MCS, GITAM University, AP, India

[2]MBBS Student, GIMSR GITAM University, Visakhapatnam, India

[3]Senior Consultant Obstetrics and Gynaecology, KIMS Trivandrum, India

[4]Travancore Medical College Quilon, India

***Corresponding Author**: Radhakrishnan Pradeep Kumar, Professor, Chief Division of Cardiothoracic and Vascular Surgery, GIMSR, GITAM University, Programme Coordinator TAH and MCS, GITAM University, AP, India.

Received: April 19, 2020; **Published:** May 04, 2020

Abstract

The most common valvular heart disease in developed nations would be aortic stenosis which affects 3% of individuals above the age of 65 years [1]. 60 - 75% narrowing from the normal valve area makes the lesion haemodynamically significant. Currently degenerative causes take preponderance over rheumatic aetiology in developed countries. Sclerotic and radiation induced lesions are also noted [2]. Initial stages remain asymptomatic due to compensatory role played by left ventricular hypertrophy and atrial augmentation of preload [3]. Heart failure angina and syncope ensues with life expectancy being shortened to approximately 3 years unless the obstruction is relieved. Asymptomatic patients, serial Doppler echocardiography is done every six to 12 months if aortic stenosis is severe, every one to two years for moderate disease, and every three to five years for mild disease. Select few may benefit by interventions prior to onset of symptoms. Transcatheter interventions have revolutionized the treatment in high or prohibitive risk category is now being extended to the moderate risk group too. Subvalvular and supravalvuar pathologies are not included in this discussion. Management of associated conditions like hypertension, coronary artery disease and atrial fibrillation is also needed. Symptoms, severity and LV response to pressure load are current deciding factors on management strategy for aortic stenosis. It can affect 6/1000 new born infants and can be diagnosed as early as 16 weeks in-utero.

Keywords: *Aortic Stenosis; TAVI; AVR; TAVR; Valve in Valve; Fetal Balloon Dilatation; CHA2DS2-VASC Score*

Introduction

There has been a better understanding of pathophysiology of aortic stenosis and paradigm shift in management strategies that have led to a better outcome in this spectrum of valvular heart pathologies. Earlier onset of the disease is noted in those with congenital bicuspid valves, disorders of calcium metabolism and renal failure and is also the most common cause of sudden death amongst valvular heart diseases. In aortic stenosis it is progressive calcification, even with lamellar bone formation that causes immobility of the valve [8]. In bicuspid valves fusion of non-coronary with right or left is noted more often than fusion of left and right cusps. Aortic root pathology may co-exist in cases with congenital bicuspid valves. A pathological process similar to atherosclerosis with lipid accumulation, inflammation

and calcification is noted in valves. Left ventricular hypertrophy leads to diastolic dysfunction and resistance to left ventricular filling [4,5]. Myocyte thickening, increased stiffness of extracellular matrix leads to increased isovolumic relaxation phase and reduced ventricular filling. Increased demand, reduced filling and compression effects on coronary arteries can lead to ischaemic symptoms in absence of coronary occlusion also. Endocardial flow may be compromised by increased chamber pressure also [6,7]. Better predictors of angina are aortic valve area and ratio of systolic ejection time to diastolic filling time. Decompensation and drop in systemic vascular resistance leads to hypotension and syncope. Elderly patients may just experience loss of exercise tolerance while classical triad may be present in the majority. Also, elderly patients murmur may be less intense with radiation to apex instead of to carotids. Valve orifice area of less than 0.6 cm^2 is noted in severe aortic stenosis. Reduction in stroke volume may be noted with normal ejection fraction with the end diastolic volume is reduced secondary to concentric remodelling. In these situations transvalvular gradients may be low. Transvalvular gradients of more than 40 mmHg being judged as severe applied only when left ventricular function is normal. Transvalvular gradient increased by square of output and hence activation of myocardial sensors leads to drop in vascular resistance during exertion explaining the syncope noted with this pathology. Exercise induced arrhythmias are also contributory factors. Both systolic and diastolic dysfunction contributes to difficulty in breathing that is experienced by the patients.

See table 1 for classification of severity of aortic stenosis.

	Transaortic velocity (m per second)	Mean pressure gradient (mm Hg)	Aortic valve area (cm^2)
Normal	< 2.0	< 10	3.0 to 4.0
Mild	2.0 to 2.9	10 to 19	1.5 to 2.9
Moderate	3.0 to 3.9	20 to 39	1.0 to 1.4
Severe	≥ 4.0	≥ 40	< 1.0

Table 1: *Classification of aortic stenosis severity classification.*

Echocardiography helps in assessment of number of leaflets, valve motion, calcification, LV function, transaortic velocity and Doppler pressure gradients. Symptoms are noted when transvalvular velocity exceeds 4.0 m/sec. With EF less than 50% diagnosis of LV dysfunction and low flow aortic stenosis must be considered. Dobutamine stress echocardiography can help in detection of causes of low ejection fraction. In Pseudo severe AS, the increase EOA with little increase of gradient in response to increase flow occurs whereas in true severe AS little or no increase EOA with increase in gradient with increase of flow is noted.

There has been a decline in interventional mortality from 5%to 2.5% [12] which is at par with the risk of sudden death in asymptomatic patients being managed medically. This has led to a revised management protocols in many countries. Asymptomatic patients with more than 1 risk factor like heavy valve calcification- indicating rapid progression of disease, transaortic jet velocity of more than 4.0 m/sec, those with abnormal exercise test, severe left ventricular hypertrophy, high levels of B type natriuretic peptide may undergo interventions at low risk centres listed out for the same. Patients with severe stenosis (transaortic velocity of at least 5.0m per second) or a rapid increase in transaortic velocity over time (0.3 m per second or more per year) with an increased likelihood of becoming symptomatic in one to two years are also better dealt with by intervention. Those who respond to inotrope augmentation in both the severe and pseudo aortic stenosis group will benefit from intervention. Asymptomatic patients with severe or moderate stenosis undergoing cardiac surgery for other indications are also better dealt with by simultaneous intervention. Clearly current concepts have clarity and notable differences from the previous management strategies for aortic stenosis.

TAVI

Transcatheter interventions have evolved over a decade now with excellent relief of obstruction. The biggest attraction is still for the high risk surgical group providing better quality of life and longevity. 30-day surgical mortality for isolated surgical valve replacement is 3% and 4.5% for valve replacement with coronary artery bypass grafting [13]. Mounting evidence for the use of transcatheter aortic valve replacement (TAVI) as standard therapy is being mooted currently with the release of data from two major new studies that demonstrate its role in low-risk patients [16]. Currently available devices are summarised in table 2. For transcatheter interventions annulus to ostial distance must be more than 12 mm. Low lying ostial will increase risk of coronary ostial occlusion. Transarterial access should be avoided with aortic tortuosity, aneurysm or protruding atheroma or thrombus. Porcelain aorta should have a lumen of adequate size for interventions by this method. Patients with mild stenosis have no activity restrictions imposed upon. Asymptomatic patients with moderate to severe stenosis should avoid competitive or vigorous activities that involve high dynamic and static muscular demands, although other forms of exercise are considered safe [14]. Diuretics have the potential to reduce diastolic filling and should be used in low doses only and peripheral alpha blockers should be avoided.

Device Name	Valve Structure	Access Route, Delivery System, and Valve Size	Reference Access Vessel Diameter	Repositionable?	Fully Retrievable?
Sapien 3 (Edwards Lifesciences)	Bovine pericardial tissue valve balloon-expandable cobalt-chromium frame	TF: Edwards eSheath 14 F (20, 23, 26 mm), 16 F (29 mm); TA, TAo: Certitude 18 F (20, 23, 26 mm), 21 F (29 mm)	≥ 5 mm (Sapien 3: 23, 26 mm), ≥ 5.5 mm (Sapien 3: 29 mm)	No	No
Evolut R (Medtronic)	Porcine pericardial tissue valve; self-expanding nitinol frame	TF, TAo, TSc: EnVeo R 14 F outer diameter (23, 26, 29, 34 mm)	≥ 5 mm (Evolut R: 23, 26, 29 mm) ≥ 5.5 mm (Evolut R: 34 mm)	Yes	Yes
Portico (St. Jude Medical, Inc.)	Bovine pericardial tissue valve; self-expanding nitinol frame	TF, TAo, TSc: 18 F (23, 25 mm) 19 F (27, 29 mm)	≥ 6 mm	Yes	Yes
Acurate Neo (Symetis)	Porcine pericardial tissue valve; self-expandable nitinol alloy stent	TF: 18 F outer diameter (small, medium, large); TA: sheathless 28 F (small, medium, large)	≥ 6 mm	No	No
JenaValve (JenaValve Technology GmbH)	Porcine pericardial tissue valve; self-expanding nitinol stent	TA: sheathless 32 F (23, 25, 27 mm)	-	Yes	No
Lotus (Boston Scientific Corporation)	Bovine pericardial tissue valve; self-expanding, braided nitinol frame	TF: 18 F (23 mm), 20 F (25, 27 mm)	≥ 6 mm (Lotus: 23 mm) ≥ 6.5 mm (Lotus: 25, 27 mm)	Yes	Yes
Allegra (NVT AG)	Bovine pericardial tissue valve (annular skirt and leaflets); self-expanding nitinol stent	TF: 18 F (23, 27, 31 mm)	≥ 6 mm	Yes	Yes

Table 2: *Current TAVI devices.*

Current indications for aortic valve replacement (surgical or transcatheter) are as follows:

1. Severe high-gradient AS with symptoms (class I recommendation, level B evidence).

2. Asymptomatic patients with severe AS and LVEF < 50 (class I recommendation, level B evidence).
3. Severe AS when undergoing other cardiac surgery (class I recommendation, level B evidence).
4. Asymptomatic severe AS and low surgical risk (class IIa recommendation, level B evidence).
5. Symptomatic with low-flow/low-gradient severe AS (class IIa recommendation, level B evidence).
6. Moderate AS and undergoing other cardiac surgery (class IIa recommendation, level C evidence).

TAVR is approved for the following:

1. Intermediate to prohibitive surgical risk patients with severe AS.
2. Valve-in-valve procedure for failed prior bio prosthetic valve.

Contraindications

Life expectancy less than 1 year due to a noncardiac cause, myocardial infarction within the last thirty days, congenital unicuspid, bicuspid or noncalcified valve, hypertrophic cardiomyopathy, need for emergency surgery, left ventricular ejection fraction less than 20%, severe pulmonary hypertension with right ventricular dysfunction, echocardiographic evidence of intracardiac mass, thrombus or vegetation, native aortic annulus smaller than 18 or larger than 25 mm, severe mitral regurgitation, MRI confirmed CVA or TIA within last six months, end-stage renal disease, mixed aortic valve disease (concomitant aortic regurgitation), or significant aortic disease [19]. Refer to table 3 for absolute contraindications for the procedure. Relative contraindications include need for concomitant coronary revascularisation, bicuspid or noncalcified valve, LVEF of less than 20%, hemodynamic instability and for apical approach non accessible LV apex and severe pulmonary disease. As technology improves many of these may disappear from the list too.

Life expectancy of less than 1 year
No expected improvement in outcome due to co morbidities
Any other surgical indications for other valvular pathologies co exist
Non availability of heart team or appropriateness of procedure not confirmed by heart team
Inadequate annulus size- as per device availability status
Thrombus in left ventricle, ascending aorta or arch
Active endocarditis
High coronary ostial occlusion risk
Access site contraindications

Table 3: *Absolute contraindications to TAVI.*

Technique

Multiple options for transcatheter aortic valves exist. Only two currently FDA-approved for use in the United States are the SAPIEN valves (Edwards Life sciences, Irvine, CA) and the CORE valves (Medtronic Fridley, MN). The SAPIEN valves have balloon expandable

bovine pericardial tissue on a chromium cobalt alloy frame. Latest Medtronic valve is the EVOLUT-R made of porcine tissue and a nitinol frame, with added advantage of being self-expandable and ability for repositioning after deployment [20-22].

Surgical interventions are best for severe lesions with low and moderate surgical risk. Mechanical valve replacements should maintain INR in range of 2 - 3 and biological valves should have antiplatelet agents being continued on follow up. Indications for the Ross procedure are children with congenital stenosis, young adults with small aortic annulus, women of child bearing age group and those with complex left ventricular outflow disease or prosthetic valve endocarditis and those with dilated aortic annulus. It is contraindicated in Marfans and those with rheumatic valve disease with a dysplastic dilated aortic root due to autograft dysfunction. Homograft valves can be considered in those with active endocarditis.

Role of heart team

There are three questions that a heart team has to answer- is percutaneous intervention acceptable for that particular patient according to current guidelines, is the anatomy suitable and of the various routes like transfemoral, transapical, axillary or transaortic which would be the best according to the patient anatomy and device selected. Here again a good clinical sense should prevail. The post evaluation heart team meeting usually includes the cardiologist and cardiac surgeon plus anaesthetist, radiologist, intensivist, geriatrician, research nurses, or any other as deemed necessary relating the patient co morbidities. The heart team takes care of in hospital management, compliance to registries and also organises the follow up. There is a need for optimal training programme with hands on experience in simulators.

Percutaneous interventions for valve in valve procedures are acceptable for the high surgical risk category where the dimensions and characteristics of failed valve are understood and compatible with good transcatheter valve function, and expected life expectancy is more than 2 years [9-11,17,18]. Left sided heart lesions can recur when one child is affected with a frequency of 4.5 to 13%. Measures of in-utero intervention [15] of aortic stenosis are available in a few select centres globally.

Coexistent CAD and atrial fibrillation

Aortic stenosis frequently coexists with coronary artery disease and the safety and feasibility of PCI in conjunction with TAVI has been well established in selected patients. Currently heat team decisions based on thoughtful discussion on an individual basis is needed till high quality randomized trial results are available. See table 4 for management options.

1- or 2-vessel CAD:

- SAVR plus coronary artery bypass grafting (CABG) is appropriate for low, intermediate, or high surgical risk;
- TAVR plus percutaneous coronary intervention (PCI) is appropriate for patients at intermediate or high surgical risk; and
- SAVR plus PCI may be appropriate in the absence of proximal left anterior descending artery (LAD) involvement.

3-vessel CAD:

- SAVR plus CABG is appropriate for low, intermediate, or high surgical risk and regardless of the SYNTAX (Synergy between percutaneous coronary intervention with Taxus and Cardiac Surgery) score; and
- TAVR plus PCI is appropriate for patients at intermediate or high surgical risk and a SYNTAX score below 22.

Left main CAD:

- SAVR plus CABG is appropriate for low, intermediate, or high surgical risk and regardless of the SYNTAX score;
- TAVR plus PCI is appropriate for patients at intermediate or high surgical risk and a SYNTAX score below 33; and
- TAVR plus PCI may be appropriate for patients at intermediate or high surgical risk and a SYNTAX score of at least 33.

Table 4: *Symptomatic severe high-gradient aortic stenosis with coronary artery disease (CAD).*

Atrial fibrillation is observed in up to a third of high risk patients undergoing percutaneous interventions on aortic valve stenosis. The risk of mortality is twofold at 1 year follow up. Among patients with AF CHA2DS2-VASC score directly co related with risk of all cause mortality. Incidence of post procedure atrial fibrillation is less 5% vs. 23% compared to surgical intervention [23].

Transformation to percutaneous routes has begun and likely to herald as the primary management strategy for other valvular disorders also in near future. The reported success rates in USA and Europe are over 90% and 30 day mortality as low as 3% [23]. Early deaths are due to arrhythmias, heart failure and pulmonary complications. TAVI with third generation devices achieve similar short and midterm survival compared with surgical interventions. Long term durability especially in younger patients is to be evaluated before extending the use of this technology to low risk group.

Long term benefits envisaged includes a higher survival advantage, better quality of life, lower reintervention rates, low transvalvular gradients with better valve areas that tips the balance in favour of percutaneous interventions in future with better technological devices.

Conclusion

Better understanding of pathology, ground breaking technologies and refinements may still create a series of refinements in tunnel of future and lead to better in-utero strategies eliminating the disease in adulthood altogether. Multidisciplinary teams with patient at the core would emerge as the most practical scenarios as technology marches ahead with variable pace amongst specialisations of medicine. With better operator experience and advanced technological expertise TAVI may soon extend its applications to low risk group also because of lower complications and quicker recovery.

Bibliography

1. Lindroos M., *et al.* "Prevalence of aortic valve abnormalities in the elderly: an echocardiographic study of a random population sample". *Journal of the American College of Cardiology* 21.5 (1993): 1220-1225.

2. Rose AG. "Etiology of valvular heart disease". *Current Opinion in Cardiology* 11.2 (1996): 98-113.

3. Grossman W., *et al.* "Wall stress and patterns of hypertrophy in the human left ventricle". *Journal of Clinical Investigation* 56.1 (1975): 56-64.

4. Hess OM., *et al.* "Diastolic stiffness and myocardial structure in aortic valve disease before and after valve replacement". *Circulation* 69.5 (1984): 855-865.

5. Hess OM., *et al.* "Diastolic dysfunction in aortic stenosis". *Circulation* 87.5 (1993): IV73-IV76.

6. Stott DK., *et al.* "The role of left atrial transport in aortic and mitral stenosis". *Circulation* 41.6 (1970): 1031-1041.

7. Ross J Jr. "Afterload mismatch and preload reserve: a conceptual framework for the analysis of ventricular function". *Progress in Cardiovascular Diseases* 18.4 (1976): 255-264.

8. Mohler ER., *et al.* "Bone formation and inflammation in cardiac valves". *Circulation* 103 (2001): 1522-1528.

9. Leon MB., *et al.* "PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery". *The New England Journal of Medicine* 363 (2010):1597-1607.

10. Smith CR., *et al.* "PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients". *The New England Journal of Medicine* 364 (2011): 2187-2198.

11. Kodali SK., *et al.* "PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic-valve replacement". *The New England Journal of Medicine* 366 (2012): 1686-1695.

12. Online STS risk calculation (2012).

13. Society of Thoracic Surgeons. Executive summary: STS spring (2015).

14. Bonow RO., *et al.* "Task Force 3: valvular heart disease". *Journal of the American College of Cardiology* 45.8 (2005): 1334-1340.

15. D Maxwell and L Allan MJ "Tynan Balloon dilatation of the aortic valve in the foetus: a report of two cases". *British Heart Journal* 65.5 (1991): 256-259.

16. "ACC 2019: TAVI moves to the mainstream with new findings in low-risk patients" (2019).

17. Mylotte D., *et al.* "Transcatheter aortic valve replacement in Europe: adoption trends and factors influencing device utilization". *Journal of the American College of Cardiology* 62 (2013): 210-219.

18. Tchetche D., *et al.* "How to make the TAVI pathway more efficient". *Inter Cardio* 14.1 (2019): 31-33.

19. Wilson R., *et al.* "Transcatheter Aortic and Mitral Valve Replacements". *Radiologic Clinics of North America* 57.1 (2019): 165-178.

20. Edelman JJ and Thourani VH. "Transcatheter aortic valve replacement and surgical aortic valve replacement: Both excellent therapies". *The Journal of Thoracic and Cardiovascular Surgery* 156.6 (2018): 2135-2137.

21. Gillam LD and Marcoff L. "Echocardiographic Assessment of Transcatheter Aortic Valve Hemodynamics: More Tools for the Toolbox". *JACC Cardiovasc Imaging* 12.1 (2019): 35-37.

22. Chetcuti SJ., *et al.* "Self-Expanding Transcatheter Aortic Valve Replacement in Patients with Low-Gradient Aortic Stenosis". *JACC Cardiovasc Imaging* 12.1 (2019): 67-80.

23. Leon MB., *et al.* "Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients". *The New England Journal of Medicine* 374 (2016): 1609-1620.

24. Stefan Stortecky and Lutz Buellesfeld. "Atrial fibrillation and aortic stenosis- Impact on clinical outcomes among patients undergoing transcatheter aortic valve implantation". *Circulation: Cardiovascular Interventions* 6 (2013): 77-84.

Volume 7 Issue 6 June 2020