Review Article

Review of transcatheter aortic valve replacement procedure in aortic valve stenosis

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Severe symptomatic aortic stenosis is one of the commonest valve diseases due to various etiologies in elderly. Surgical aortic valve replacement (SAVR) was the treatment of choice in such cases. Transcatheter aortic valve replacement (TAVR) is the new alternative for patients with symptomatic severe aortic stenosis for whom traditional open chest surgery has intermediate or high risk. TAVR is less invasive with very short hospital stay. With availability of technical expertise and newer generation valves both the short term and long term results have significantly improved. Paravalvular leak after TAVR is quite common with first generation valves. But in newer generation valves with longer skirts the incidence of aortic regurgitation has come down. Vascular sequelae are independent predictors of death, largely attributed to the wider sheaths (inner diameter, 24F. 26F) required by earlier-generation devices. As the sheath sizes decrease with the new generation devices (14 F-equivalent system) the rate of vascular sequelae and the incidence of bleeding continue to decrease. India is very promising with percutaneous valve replacement therapy for other indications and other valves evolving fast.

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Severe symptomatic aortic stenosis is one of the commonest valve diseases due to various aetiologies in elderly[1]. When asymptomatic aortic stenosis starts to develop symptoms, there overall life expectancy decreases accordingly. Surgical AVR was the treatment of choice in these cases. But its utility is limited in patients with higher operable risk due to substantial periprocedural risk[2].In 1985, Cribier *et al* performed the first aortic valve balloon valvuloplasty in an inoperable 77 year old who had severe symptomatic aortic stenosis. The procedure resulted in reduction in aortic valve gradientand improvement in quality of life. This laid the foundation of transcatheter aortic valve procedures in high risk severe symptomatic aortic stenosis. In 2002, cribier *et al*, demonstrated the first trancatheter aortic valve replacement in inoperable high risk 57 year old patient who had undergone balloon valvuloplasty one week prior. He underwent emergency transcatheter aortic valve replacement with good immediate result.The implanted device exhibited an excellent hemodynamic performance during the first 9 weeks of follow-up. The patient died at the fourth month of follow up because of noncardiac cause.

Three years later, Paniagua *et al* performed the first TAVR through the retrograde route. The deployed device was implanted through the transfemoral access. Although the valve seemed to function well and there was an initial improvement in patient clinical status, the third postprocedural day the patient suddenly developed respiratory distress and refractory hypotension and was treated for pulmonary embolism but he died 2 days later.

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Evidence from Trials :

Results from various trials have shown transcatheter aortic valve replacement (TAVR) has better result over surgical aortic valve replacement (SAVR) in patients with symptomatic severe aortic stenosis. Over a period of time interventional cardiologists have become better with the techniques and the complication rates have reduced due to advancements in the hardwares. The Placement of Aortic Transcatheter Valves (PARTNER) Cohort B study evaluated the TAVR in inoperable patients and showed that patients treated with TAVR had a lower mortality rate compared with those treated only with medications, or with medications and balloon aortic valvuloplasty (20.5% mortality in the TAVR group at 1-year follow-up versus 44.6% in the control group; hazard ratio, 0.39; 95% confidence interval, 0.27–0.56; P<0.001)[3]. PARTNER 1cohort A trial compared TAVR and SAVR in high operative risk patients[4]. There were no differences in mortality at 1- (24.2% for the TAVR sub-group and 26.8% for the SAVR sub-group; P=0.44) and at 2-year follow-up (33.9% for the TAVR arm and 35.0% for the SAVR arm; P=0.78), those undergoing TAVR were likely to have a neurological event (11.2% *versus* 6.5%; P=0.05) or major vascular complications (11.6%

versus 3.8%; P<0.001), whereas the patients treated with SAVR demonstrated higher major bleedings (29.5% versus 19%; P=0.002) at 2-year follow-up.

CoreValve US Pivotal extreme risk iliofemoral study that included 471 high-risk patients (with a >50% predicted operative mortality or serious irreversible morbidity at 30 days) implanted with the CoreValveprosthesis (Medtronic Inc) demonstrated thatTAVR is associated with improved outcomes in this inoperable population[5].Due to better operator experience and improved transcatheter valve systems which have led to a worldwide trend to use TAVR in patients who are at intermediate risk. Placement of Aortic Transcatheter Valves (PARTNER) 2 cohort A randomized trial, in which TAVR with a second-generation valve system was compared with conventional open heart surgery in patients with severe aortic stenosis and intermediate-risk clinical profiles.The results of PARTNER 2 showed TAVR, performed in experienced centers, with the use of a lower-profile, next-generation device, was noninferior to surgery with respect to outcomes at 2 years (death from any cause or disabling stroke). Second, bioprosthetic-valve gradients were lower and the areas were greater with the SAPIEN XT valve, as compared with surgical valves, whereas the incidence of paravalvular aortic regurgitation was higher after TAVR than after surgery. Third, several benefits with regard to secondary end points were associated with TAVR, including lower risks of bleeding events, acute kidney injury, and new-onset atrial fibrillation, as well as more rapid early recovery that resulted in shorter durations of stay in the ICU and hospital.

Safety and Efficacy Study of the Medtronic CoreValve System in the Treatment of Severe, Symptomatic Aortic Stenosis in Intermediate Risk Subjects Who Need Aortic Valve Replacement SURTAVI trial evaluated TAVR vs SAVR in intermediate risk population and results showed TAVR was non-inferior to SAVR in these group of patients . In this trial Evolut R bioprosthesis was used. In this study the overall mortality were the same. However acute kidney injury, atrial fibrillation and transfusions were more in surgical group.

PARTNER trial 3 is ongoing with Edwards sapien 3 valve in patient with severe aortic stenosis in low risk group according to STS scores.

TAVR Indications :

Patients with severe symptomatic valvular aortic stenosis with an echo derived mean gradient >40mmhg

High or intermediate surgical mortality as assessed by Euroscore and STS scores (Fig 1, Table 1).

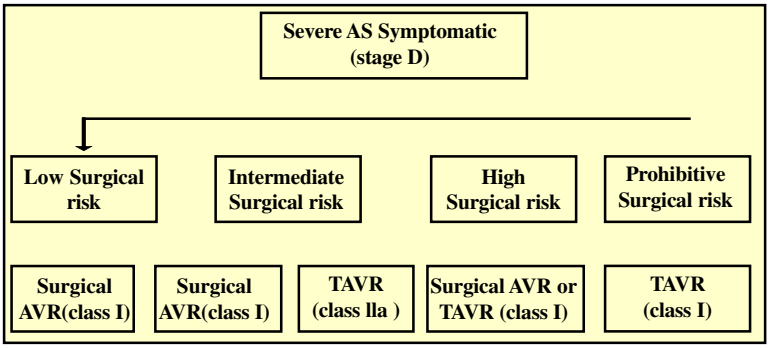

Fig 1 — Flow chart for management of aortic stenosis (ACC/AHA 2017)

Table 1 — *Recommendations and level of evidence for management of aortic stenosis*

Recommendations	Class of Recommendation	Level of Evidence
TAVR is recommended for symptomatic severe (AS stage D) and a prohibitive risk for surgical AVR who have a predicted post TAVR survival more than 12 months	I	A
Surgical AVR is recommended in patients with severe AS (stage D) and asymptomatic patients with severe AS (Stage C) who meet an indication for AVR in when surgical risk is low or intermediate	I	B
TAVR is reasonable alternative to SAVR for surgical patients with severe AS(stage D) and an intermediate surgical risk	IIa	B
Percutaneous aortic balloon dilatation can be considered as bridge to surgical AVR or TAVR in symptomatic sever AS (Stage D)	IIb	C
TAVR is not recommended in patients whom existing comorbidities would precludethe expected benefit for correction of AS	III	B

Pre-TAVR Evaluation:

For selection of patients for the procedure a detailed clinical evaluation, routine lab values chest xray, trans thoracic echo, PFT, carotid ultrasound , coronary angiography and CT Angiography of the aortic valve, chest, abdomen and pelvis.

After confirmation of diagnosis and severity of aortic valve disease by clinical examination and echocardiography, patient undergoes risk assessment for surgical aortic valve replacement. Standard risk scores include STS score and Euro score which can assessed quickly. Also mini mental examination and frailty index are assessed prior to the procedure.

The patient is then discussed thoroughly by the heart team which consists of interventional cardiologists, imaging specialists, heart surgeons and cardiac anesthesiologists.

Transthoracic and transesophageal echocardiography have been found inferior to real-time 3-dimensional imaging for measuring annular size[6].Multidetectorcomputed tomography has proved to be the method of choice for pre-TAVR evaluation of the suitability of iliofemoral access and for detailed anatomic evaluation of the aortic root and valve annulus. CT angio helps to assess the aorto iliac patency, calcification and tortuosity. This is of utmost importance because the presence of occlusive PAD, small vessels and excessive torsuosity would preclude a trans femoral approach.MDCT also helps in assessment of coronary arteries prior to surgery[7,8]. Left- and right-sided heart catheterization areused to evaluate coexisting coronary artery disease andpulmonary hypertension; pulmonary function testsare also part of the routine pre-TAVR evaluation.

TAVR Procedure :

The major advantage of TAVR is the fact that owing to its minimum invasive nature it can be done in patients who are too surgically moribund to undergo open surgery.

A team of interventional cardiologists and imaging specialists, heart surgeons and cardiac anesthesiologists work together, utilizing fluoroscopy and echocardiography to guide the valve to the site of the patient's diseased heart valve.A catheter is placed in the femoral artery (in the groin) similar to angioplasty, and guided into the chambers of the heart. A compressed tissue heart valve is placed on the balloon catheter and is positioned directly inside the diseased aortic valve. The commonest site of implant is through the femoral route. The other less frequently employed route is subclavian and direct aortic.There are two types of valves commonly used , the self expanding Medtronic Core/Evolut R Valve and the balloon expandable Edwards Sapien 3 valve. The newer valves are also advantageous because of its smaller delivery system (14-18F). The native valve is crossed retrogradely from the aorta to the left ventricle. Baloon aortic valvuloplasty is usually performed prior to valve implantation with undersized balloon during rapid ventricular pacing. After the predilatation, transcatheter valve is introduced and appropriately positioned under fluoroscopic guidance and deployed. Balloon expandable valves require rapid pacing during deployment and self expanding valves usually do not require rapid pacing during deployment.

Once the valve is deployed, the valve function is assesd by aortography, hemodynamic pressure assessment and by echocardiography (Transoesophageal echocardiography whenever available). Simultaneous LV -Aorta gradient helps to assess the gradient and also the AR index (to assess paravalvular leak).

Current Status of TAVR in India :

Since the initial TAVR in 2002, globally over 3,00,000 procedures have been performed. Few centres in India including ours started TAVR early since 2014-15. Initial we had to get individual patient licence and import the valve. But since august 2016, two important transcatheter valves namely Medtronic Evolut R valve and Edwards Sapien 3are approved by DCGI and available in India. Till the end of 2017, around 350 TAVR procedures have been performed in India and is expected to further grow in India. Major centres in India performing TAVR are in New Delhi, Japiur, Bangalore and Chennai. In Chennai, less invasive TAVR has been recently started by us (authors) using local anaesthesia, short hospital stay and using proglide sutures for the groin without vascular cut down of the artery.

TAVR and Heart :

TAVR helps in alleviating theincrease in LV pressure load and improves LV hemodynamic performance[9].It normalizes ventricular-arterial coupling, decrease left ventricular hypertrophy, and improve LV systolic function in patients with LV dysfunction[10,11]. Elevated left-sided filling pressures in severe AS can lead to severe pulmonary hypertension in nearly one third of cases and those who underwent TAVR were found to have a reduction in pulmonary hypertension[12]. Although these results were reciprocated by balloon aortic valvuloplasty in the short term, the pulmonary pressures returned to preprocedural levels in the long term. Transthoracic echocardiograms from 95 patients evaluated before and after implantation of Edwards Sapienvalves at selected intervals in the TRanscatheter EndoVascular Implantation of VALves (Revival) trial revealed the mean valvearea (1.6 cm^2) achieved after TAVR to be comparable to that achieved by SAVR, and the clinical improvements to be sustainable at 1 year[13]. Despite slight progression of the aortic regurgitation at 1 year, most patients hadimprovement in LV structure and function[14].

Complications of TAVR:

The Valve academic research consortium(VARC), has proposed standard end points for the TAVR trials[15,16]. It has standardised postoperative sequalae of TAVR.The clinical benefit endpoints proposed by VARC are exercise performance, the judgment of NYHA functional status, and performance on various quality-of-life and frailty questionnaires. The creatine kinase-myocardial band was recommended as a periprocedural marker for myocardial infarction with a 2nd-sample equirement of a greater-than-20% increase and a 2nd-sample elevation of at least 10 times the upper limit of normal.

Transcathether AVR is associated with highest incidence of stroke post operatively among percutaneous inteventions ranging from 4 to 8%. But with the improvements in techniques, valve features and anticoagulation after procedure, the rate of ischaemic events have been

brought down.

Coronary artery obstruction due to valve obstruction is an important cause of mortality. Meticulous planning with CT aortogram and using appropriate valve size, retrievable valves can alleviate this complication.

Conduction abnormalities and need for pacemaker post TAVR was around 10-15 % in trials. It is due to the deeper implantation of valve in the left ventricle outflow tract. With more and more procedures being done with meticulous planning rate of conduction abnormalities can be brought down and there by need of pacemakers.

Paravalvular leak after TAVR is quite common with first generation valves. But in newer generation valves with more longer skirts the incidence of aortic regurgitation has come down.

Vascular sequelae are independent predictors of death, largely attributed to the wider sheaths (inner diameter, 24F–26F) required by earlier-generation devices[17].As the sheath sizes decrease with the newgeneration Edwards Sapien[3] system (inner diameter, 14F–16F) and the CoreValve Evolut R (14 F-equivalent system), the rate of vascular sequelae and the incidence of bleeding continue to decrease[18,19].

Conclusion :

TAVR is the new alternative for patients with symptomatic severe aortic stenosis for whom traditional open chest surgery has intermediate or high risk. This minimally invasive procedure replaces the narrowed aortic valve without a major surgery. With mounting scientific evidence, TAVR is now guideline recommended treatment option for patients with aortic stenosis. With availability of technical expertise and newer generation valves have significantly improved both the short term and long term results. TAVR centres of excellence are now available in few cities across India giving excellent results in par with global centres. Recently less invasive TAVR with very short hospital stay have started in India. Future in India is very promising with percutaneous valve replacement therapy for other indications and other valves evolving fast.

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