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Chapter 37

Why Can't We Extrapolate Degenerative Valve Disease to Rheumatic Valve Disease During Percutaneous Interventions?

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Abstract

Heart valve diseases constitute a major cause of cardiovascular (CV) morbidity and mortality worldwide. Percutaneous intervention of the valves has revolutionized the way various cardiac pathologies are treated. Catheter-based valve therapies came into vogue to manage those subsets of patients who are deemed to be at excessive surgical risks with significant comorbidities. It was initially indicated in an octogenarian frail patient with severe calcific aortic valve stenosis (AVS) who is at high risk for surgery with high Society of Thoracic Surgery (STS) score; but with the passage of time, the indications have widened now, even low risk is also considered for transcatheter aortic valve implantation (TAVI). Hence, it may be imperative to see the possibility of using transcatheter technologies in rheumatic valve disease. However, these technologies are expensive and require expertise, to treat the diverse substrates with variations in anatomy and pathologies, encountered in both rheumatic and degenerative heart valves, leading to many inherent technical challenges in seamlessly extrapolating it. The suitable engineering and technical changes in two valve structures for two different pathologies may make it feasible and doable; hence, more research work is required in that direction before it can be extrapolated to obtain similar outcomes.

INTRODUCTION

Catheter-based therapy, such as balloon valvuloplasty, has been in clinical use for over three decades. Newer transcatheter valve technologies have dramatically altered the approach in degenerative aortic stenosis, mitral insufficiency and congenital or postsurgical pulmonic valve disease **(Fig. 1)**.

The first TAVI was performed on April 16, 2002, by Dr Alain Cribier.[1] With the success of TAVI over the last decade, considerable interest has been generated to find other transcatheter technologies specifically designed to repair or replace native mitral, tricuspid and pulmonary valves. However, their anatomy and pathophysiology of the disease process is different and often complex, leading to various engineering challenges.

ROLE OF TRANSCATHETER INTERVENTIONS IN AORTIC VALVE DISEASE

The first catheter-based approach was balloon aortic valvuloplasty (BAV), performed in 1985 on a 77-year-old

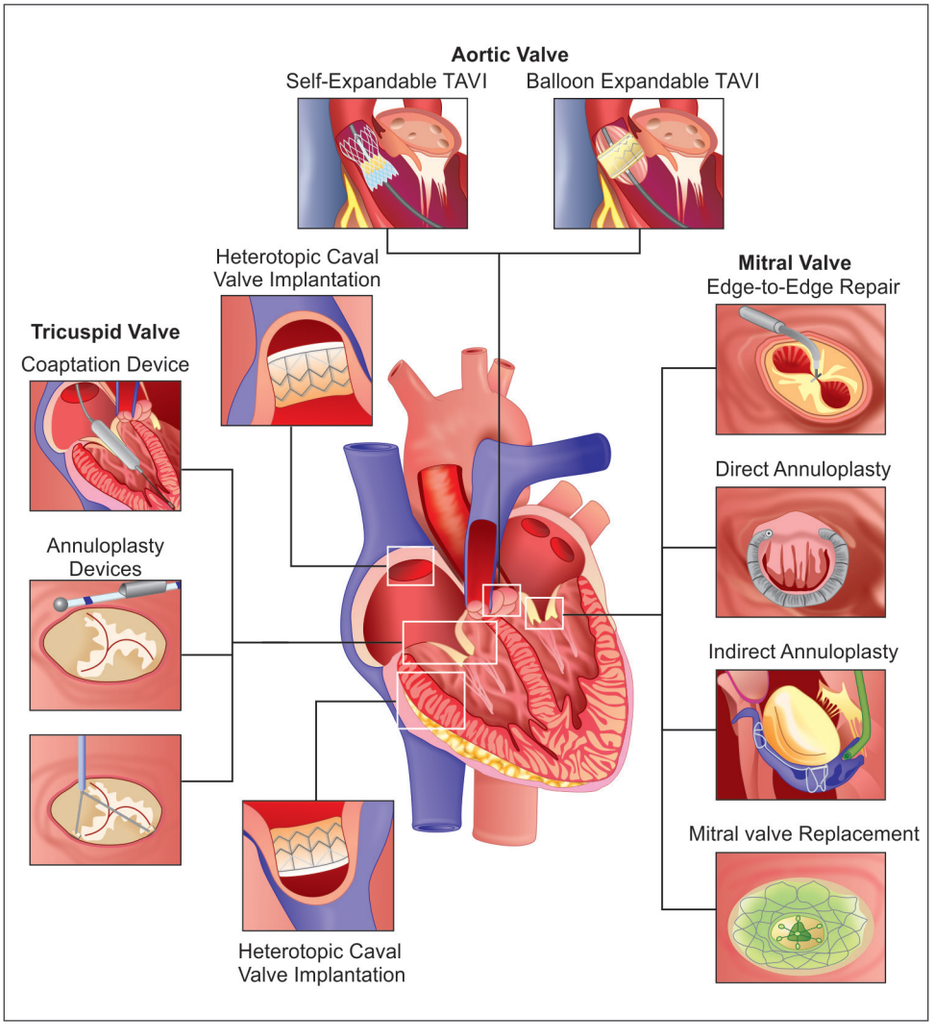
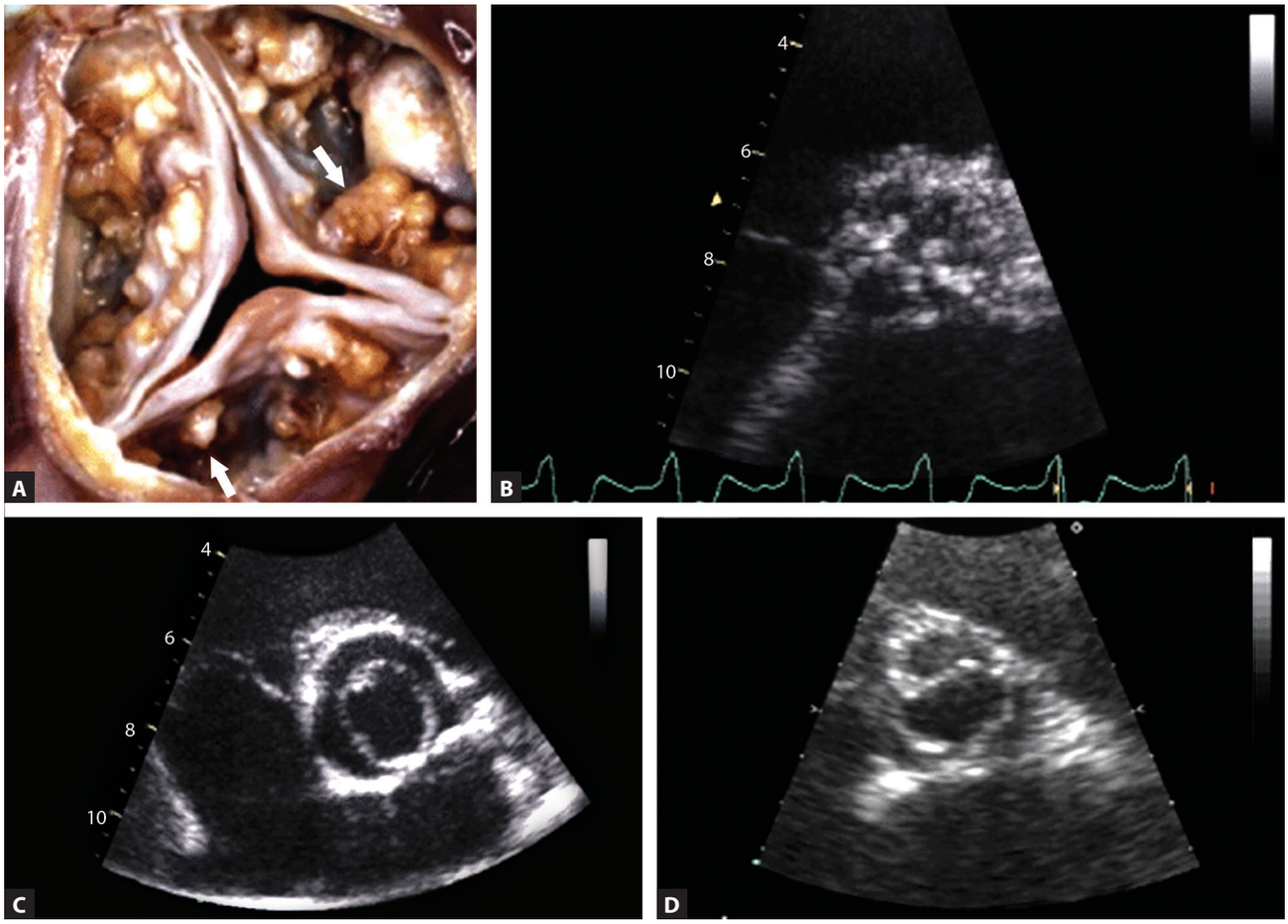


Fig. 1: Current scope of various transcatheter interventions (permission from Prendergast).

woman with inoperable severe AVS. The main limitation of this procedure was valve restenosis, which affected most patients within one-year postintervention.[1] BAV has also been attempted in rheumatic AVS with favorable results.[2]

The TAVI was later developed and is now an established treatment in patients with severe AVS, who are considered inoperable or at high surgical risk.[3] It is also becoming an attractive alternative in intermediate[4] and in low-surgical-risk patients.[5] With global experience, TAVI has also been used in some off-label indications, such as bicuspid aortic stenosis,[6] noncalcific AVS,[7] pure aortic regurgitation[8] and degenerated surgical bioprosthesis as valve-in-valve TAVI.[9] However, a high prevalence of rheumatic valve disease, high calcium burden of stenotic aortic valve leaflets, smaller aorta and peripheral vessel size, and low coronary ostia are some of the procedural impediments, commonly seen in the Indian population, resulting in higher procedural complications.

The role of TAVI in rheumatic aortic valve disease is controversial. Isolated rheumatic aortic stenosis is rare and predominantly seen in underdeveloped countries, where access and affordability are a concern. Research to develop various transcatheter valves is mainly done in the Western countries where disease pattern is predominantly degenerative. However, in the Asian countries, rheumatic valve disease is more commonly seen. Hence, the results achieved in degenerative valves cannot be compared to rheumatic valve disease. Pathology of the rheumatic aortic valve is distinct, with leaflet thickening and fibrosis,



Figs. 2A to D: (A) Photograph of the calcified aortic valve with commissural sparing. Echocardiographic appearance (parasternal short-axis views) of aortic stenosis in (B) severe calcific degenerative disease, (C) bicuspid aortic valve, (D) rheumatic disease with commissural involvement.

commissural fusion without significant calcification **(Figs. 2A to D)**. This can lead to difficulty in anchoring the valve into position. Furthermore, there is a paucity of information regarding its usage in younger patients who continue to have low-grade valve inflammation in rheumatic heart disease (RHD). There are very few reports of TAVI in rheumatic aortic valve disease.[10,11]

Gunasekaran et al. describe a case of a 70-year-old female with a history of mitral valve surgery on two previous occasions, presenting with symptomatic severe rheumatic AVS. Due to high surgical risk, TAVI was performed with SAPIEN 3 valve (Edwards Lifesciences). The procedure was successful without any paravalvular leak or valve dysfunction at six months.[12]

Brennan et al. reported a single-center TAVI procedural experience and clinical outcomes in 907 patients; of whom, 19 (2%) cases had rheumatic aortic valve disease, between February 2008 and August 2018 and TAVI was done in all 19 rheumatic valve disease patients with significant AVS and results revealed that there was no significant difference in mortality rates in two groups, at 30 days, 1, 2 and 5 years compared to conventional degenerative TAVI patients (5% vs 3%, 11% vs 13, 31% vs 19%, and 48% vs 48%, $p > 0.05$).[13]

Though the above studies have been encouraging, problems of using TAVI in rheumatic valve disease persist and cannot be compared to results achieved in degenerative valves and larger studies will clarify the

differences in performance. Performing TAVI using fluoroscopy and echocardiography is more challenging in rheumatic valves, due to paucity of calcification, often leading to valve malposition. The exact mechanism of the transcatheter valve expansion when deployed within a rheumatic aortic valve, is not known. Further studies are needed to ascertain, if there is an actual "split" in aortic commissures, like in mitral valvuloplasty or merely a stretch in the aortic annulus to accommodate the new valve.

ROLE OF TRANSCATHETER INTERVENTIONS IN MITRAL VALVE DISEASE

Balloon mitral valvuloplasty was first introduced in 1984 by a surgeon, Dr Kanji Inoue, to treat mitral valve stenosis.[14] The concept of balloon dilatation was derived from the surgically closed commissurotomy. The initial clinical experience was characterized by frequent incidence of procedural complications such as severe mitral regurgitation (MR). As more experience was gained and patient selection perfected, acute complications of balloon mitral valvuloplasty have become rare.

With a decreasing incidence in mitral stenosis (MS) due to RHD and good clinical outcomes with heart surgery, primary MR is now treated with surgery. With the aging of the population, comorbidities also increase, resulting in significant risks for surgery. This has stimulated the development of new transcatheter options in high-surgical-risk patients.

Transcatheter mitral valve intervention was introduced more than a decade ago, but its use has lagged behind TAVI, due to the complexity of the mitral valve. Understanding the pathophysiology and natural history of the disease before and after transcatheter mitral valve therapies requires long-term collaboration with echocardiographers and heart failure (HF) specialists. Devices for the treatment of calcific MS, primary and functional MR have been developed and are currently being evaluated in various clinical trials.

Transcatheter mitral valve devices can be grouped into three categories: mitral annuloplasty, mitral leaflet repair (using Alfieri technique) and total mitral valve replacement device. Among all the mitral devices in the study, the largest clinical experience is with the MitraClip, also under investigation are Edwards PASCAL mitral valve repair system, Carillon mitral system, Cardioband annuloplasty system and mitral valves prosthesis (Tendyne, CardiAQ, Tiara, Edwards Fortis, and Intrepid valve) **(Fig. 4)**.

Early trials have established the safety and feasibility of mitral valve repair using the MitraClip system in patients at high surgical risk, with improvements in dyspnea and low rates of procedure-related adverse events and mortality.[15,16] In the Endovascular Valve Edge-to-Edge Repair Study (EVEREST) II clinical trial, a comparison was made to conventional surgery at 12 months, showed that though the percutaneous repair was less effective at reducing MR than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical outcomes.[17]

The recently concluded COAPT trial showed that transcatheter mitral valve approximation using the MitraClip on a background of maximally tolerated Guideline Defined Medical Therapy (GDMT) was superior to GDMT alone in reducing HF hospitalization and mortality in symptomatic HF patients with grade 3-4 + MR.[18]

The technical challenges in using transcatheter mitral valve replacement (TMVR) are significantly more than TAVI, as it requires a trans-septal puncture and balloon atrial septostomy to deliver the mitral valve to point of interest. The septal defect made is often large and may require device closure, making the procedure more demanding and cumbersome.

The role of transcatheter interventions in rheumatic mitral valve disease is not well defined. Percutaneous mitral commissurotomy [balloon mitral valvotomy (BMV)] is still the most commonly done procedure in MS. Commissural fusion complications mitral, valve fibrosis, deformity, shortening, and subvalvular involvement are the hallmarks of mitral valve disease **(Fig. 3)**. This unfavorable anatomy makes it difficult to deploy transcatheter valve technologies like the MitraClip. Poor mitral annular anchoring, device migration and left outflow tract obstruction are some of the complications of mitral valve replacement devices. Furthermore, deploying the annuloplasty device in coronary sinus often leads to inadequate force generation, leading to suboptimal reduction of the mitral annulus. It can also cause compression of the left circumflex artery which is at close proximity, leading to coronary ischemia.

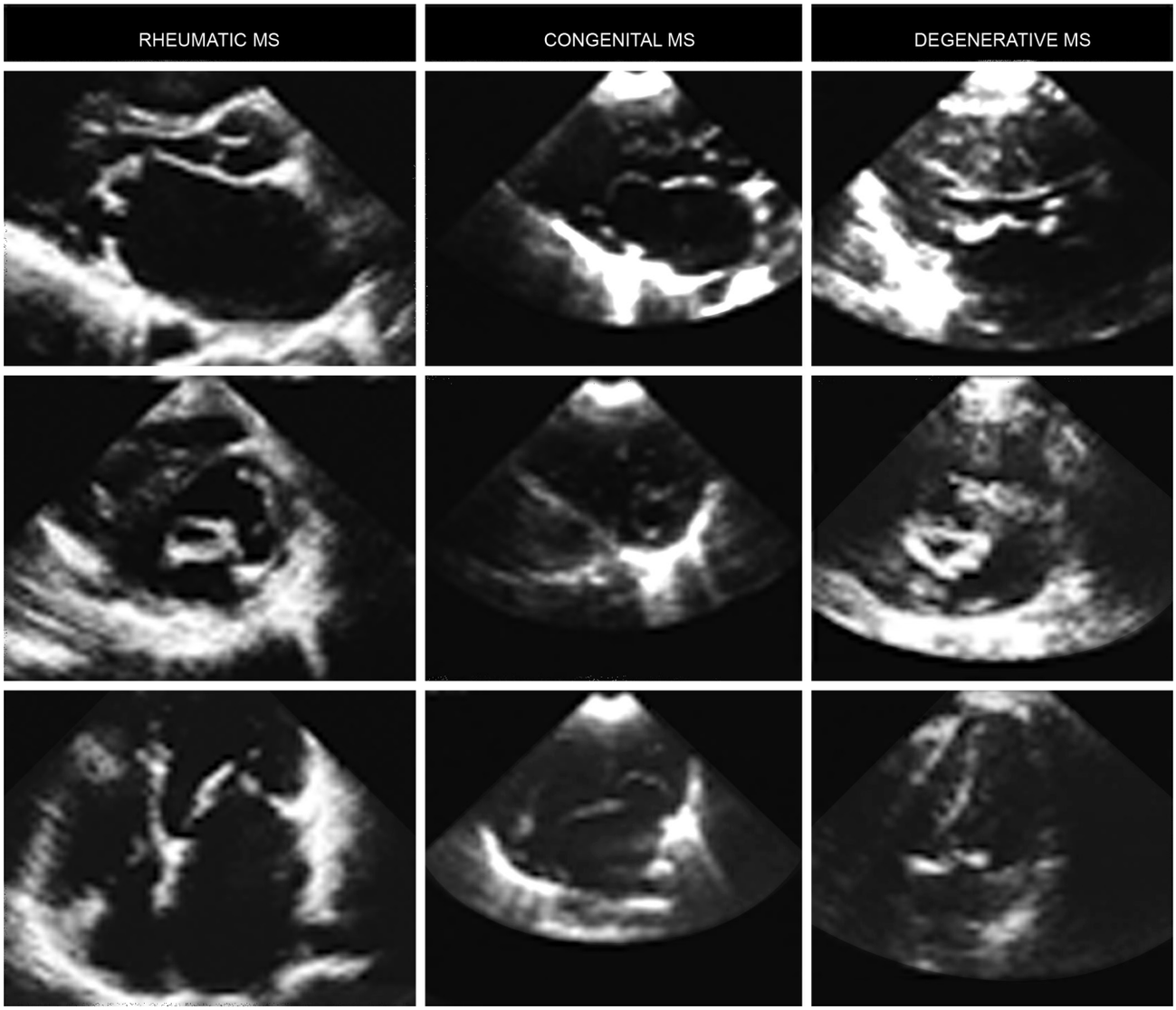


Fig. 3: Rheumatic mitral stenosis: Showing doming of the anterior mitral leaflet, fish mouth orifice with the dilated left atrium. Congenital mitral stenosis: Anterior mitral leaflet doming with the eccentric location of the orifice with both leaflets attached to the single papillary muscle. Degenerative mitral stenosis: Dense calcification, restricted opening with sparing of commissures.

ROLE OF TRANSCATHETER INTERVENTIONS IN TRICUSPID VALVE DISEASE

Tricuspid valve involvement is rare and is usually associated secondary to left-sided heart diseases. Causes of tricuspid valve disease include congenital conditions, such as Ebstein's anomaly and acquired causes like rheumatic disease, endocarditis, radiation, and carcinoid disease. Tricuspid regurgitation (TR) is seen in approximately 80% of cases and is functional, related to tricuspid annular dilation and leaflet tethering, due to right ventricular (RV) remodeling caused by pressure and/or volume overload. Surgical repair is rarely performed as an independent procedure. Experience with percutaneous tricuspid valve interventions is limited.

Fig. 4: Various transcatheter mitral valves under development. (N Piazza, Montreal, Canada)

Edge-to-edge repair (MitraClip), tricuspid annuloplasty (Trialign, TriCinch and Cardioband system), heterotopic caval valve implantation (TRIC valve and Edward SAPIEN XT valve), coaptation enhancement (FORMA repair system) and percutaneous tricuspid valve replacement (Edward SAPIEN XT) are some of the techniques and devices under investigation for functional TR **(Fig. 5)**.[19-21]

The tricuspid valve is nonplanar and a dynamic structure, whose size and shape changes with every phase of the cardiac cycle. The anatomical challenges during interventions are mainly due to large annular size, the fragility of the valve tissue, paucity of annular or valve calcification, proximity to the right coronary artery, atrioventricular node and right bundle of His branch.

The role of transcatheter interventions in the rheumatic disease of the tricuspid valve is similar to the mitral valve. Percutaneous tricuspid balloon valvuloplasty has also been attempted in symptomatic severe tricuspid valve stenosis with good results.[22,23] However, other techniques have not shown any favorable outcomes. Fibrous thickening of the leaflets, fusion of commissures, shortened chordae, small annulus and absence of calcific deposits, are some of the impediments to a successful transcatheter intervention, in valves of rheumatic etiology. Hence, the clinical outcomes in rheumatic valve disease are inferior to degenerative valve disease.

ROLE OF TRANSCATHETER INTERVENTIONS IN PULMONARY VALVE DISEASE

Valvular pulmonic stenosis is usually congenital. Acquired causes of native pulmonary valve disease are rare and may be associated with rheumatic fever, infective endocarditis or carcinoid. Percutaneous balloon pulmonary valvuloplasty, first described in 1982 by Kan, has shown good results in pulmonary valve stenosis. Pulmonary valve implantation was the first percutaneous intervention for the treatment of regurgitant lesions in humans.[24,25]

The Melody Valve (Medtronic) and Edwards SAPIEN valves are currently in use for the management of pulmonary regurgitation after surgical repair of tetralogy

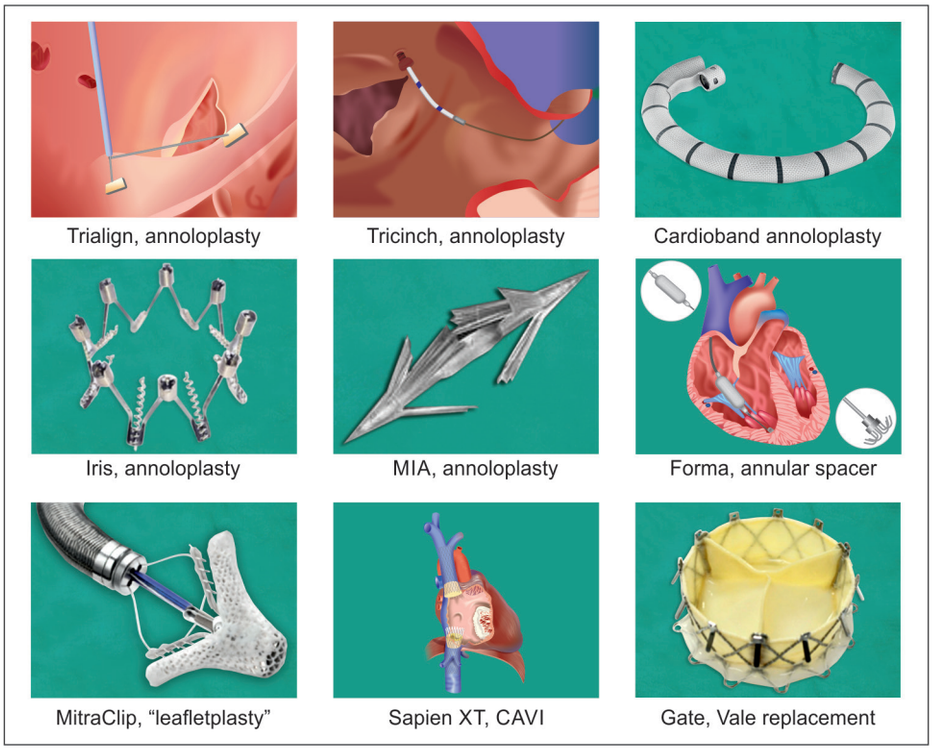


Fig. 5: Various tricuspid technologies under study.

of Fallot patients or in surgically implanted dysfunctional conduits, with off-label use in native dysfunctional RV outflow tract. Other technologies under study are Venus P-Valve,[26] Harmony,[27] and Pulsta™ transcatheter pulmonary valve.[28]

Transcatheter intervention in rheumatic pulmonary valve disease has not been reported.

CONCLUSION

In India, various surveys show a declining trend in the prevalence of RHD, but rheumatic involvement continues to be the most dominant part of valvular heart disease. However, other causes, like degenerative valves, are also on ascendancy due to the increase in average life expectancy.

Though transcatheter valve interventions have transformed the management of valvular heart diseases, there are a few problems in the implementation of the program **(Fig. 6)**. With further developments in the technology and cost reduction, majority of patients may be treated by transcatheter valves, within the next decade, alleviating the need for open heart surgery.

Transcatheter technologies are constantly evolving to address the various uncertainties concerning outcomes of the procedure such as valve durability, rhythm disorders, thrombosis, paravalvular leak, stroke/transient ischemic attacks, and optimal antithrombotic therapies.

The rheumatic and degenerative heart valve disease are two distinct entities with different pathophysiology, clinical spectrum, and presentation. Transcatheter techniques and devices that are effectively used in degenerative valve disease cannot be extrapolated seamlessly to rheumatic valve disease until the suitable engineering and technical changes commensurate in valve structure to successfully deploy the catheter valves in rheumatic valve disease with similar outcomes. This will require more research, clinical studies with data, to configure their use in RHD, owing to fundamental differences between two pathologies; but in time to come, catheter valve therapies may be the futuristic technologies for all valve pathologies.

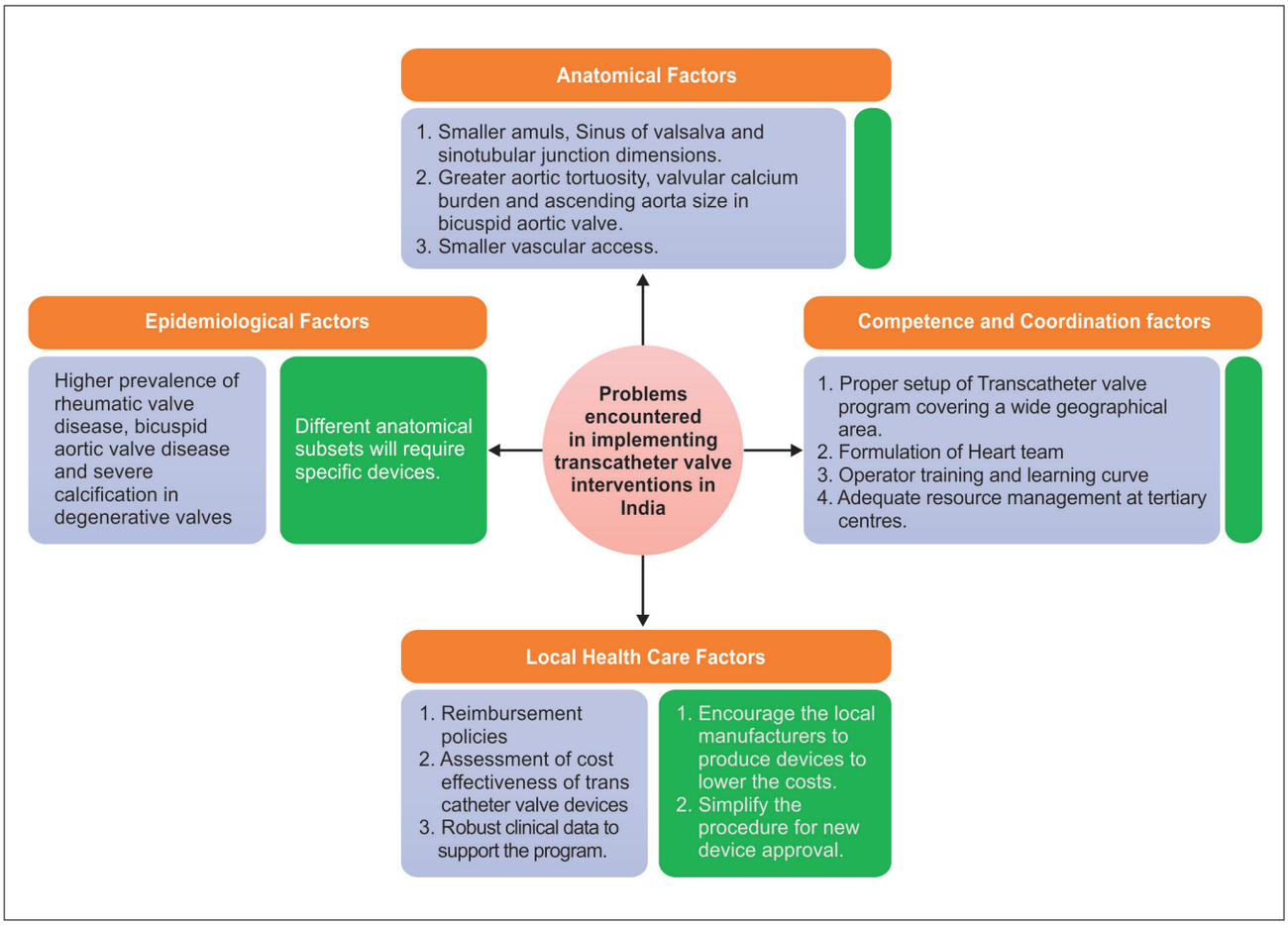


Fig. 6: Factors affecting the success of transcatheter valve interventions in India

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