

TAVI device selection: time for a patient-specific approach

Marcus Lee¹, MB; Thomas Modine², MD, PhD, MBA; Nicolo Piazza³, MD, PhD; Darren Mylotte^{1*}, MB, MD

1. Department of Cardiology, University Hospital Galway, Galway, Ireland; 2. Department of Cardiology, Hôpital Cardiologique, CHRU de Lille, Lille, France; 3. Department of Interventional Cardiology, McGill University Health Centre, Montreal, Quebec, Canada

Abstract

Individualised, patient-centred care is a central tenet of modern medicine. The variety of transcatheter heart valves currently available affords the opportunity to select the most appropriate device for each individual patient. Prosthesis selection should be based on operator experience and pre-procedural multimodal three-dimensional imaging. Herein, we outline a number of clinical scenarios where specific transcatheter heart valve technologies have the potential to optimise clinical outcome.

Introduction

Until recently, most centres performing transcatheter aortic valve implantation (TAVI) used a single prosthesis type. While this practice appears somewhat restrictive given the fact that the same centres probably implant a variety of drug-eluting stents, pacemakers, and surgical heart valves, the relative infancy of TAVI has mandated that centres become proficient in one technology at a time.

Of course, the transcatheter heart valve (THV) landscape has changed considerably in recent years and TAVI is now considered to be a standardised, mature therapy, with hundreds of thousands of treated patients worldwide. Refined patient selection, pre-procedural anatomic assessment with multislice computed tomography (MSCT), growing operator experience, the

emergence of new valves supported by prosthesis-specific education and proctoring, and relentless iteration of the foundation devices have manifested impressive reductions in procedural mortality, vascular complications, paravalvular leak, and other adverse events. In particular, the availability of an array of new THV systems (**Figure 1**), each with unique technical features and potential advantages, coupled with a much greater understanding of individualised patient anatomy, has afforded the TAVI operator the opportunity to develop a more patient-centric approach to TAVI.

It is important to acknowledge that introducing a second or third transcatheter technology to a centre can be challenging. Unlike coronary stents, each THV system has unique features that must be mastered, and the devices can react differently in diverse anatomies and clinical situations. Device-specific education and training for physicians and allied staff is required, and a period of proctoring is essential. Nevertheless, a learning curve can be expected as staff acclimatise to the new technology. It is also questionable whether low-volume centres (<30 TAVI per annum) have sufficient experience to use multiple technologies safely.

While most patients can be treated successfully with a single balloon-expanding, self-expanding, or mechanically expanding THV system, specific situations do arise where the availability of

*Corresponding author: Department of Cardiology, Galway University Hospital, Newcastle Road, Galway, Ireland.
E-mail: Darrenmylotte@gmail.com

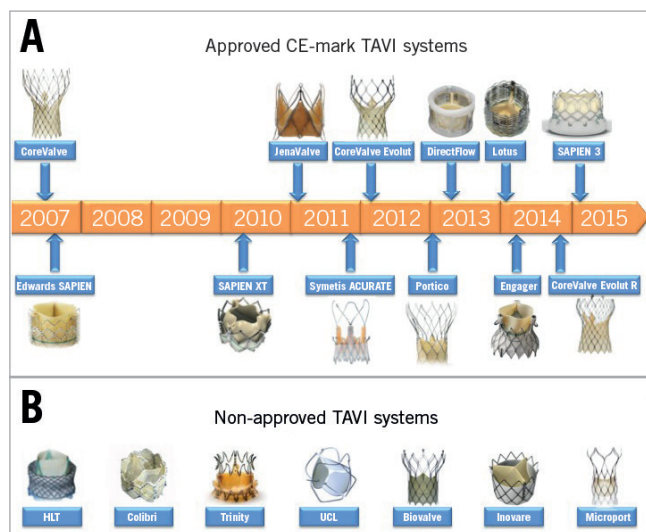


Figure 1. *Approved and non-approved TAVI devices. A) CE-mark TAVI systems. CoreValve® (Medtronic, Dublin, Ireland); SAPIEN (Edwards Lifesciences, Irvine, CA, USA); SAPIEN XT (Edwards Lifesciences); JenaValve (JenaValve Technology GmbH, Munich, Germany); Symetis ACURATE™ (Symetis SA, Ecublens, Switzerland); CoreValve® Evolut™ (Medtronic); Portico™ (St. Jude Medical, St. Paul, MN, USA); Direct Flow Medical Aortic Valve™ (Direct Flow Medical Inc., Santa Rosa, CA, USA); Lotus™ (Boston Scientific, Marlborough, MA, USA); Medtronic Engager™ (Medtronic); SAPIEN 3 (Edwards Lifesciences); CoreValve Evolut R (Medtronic). B) Non-approved TAVI systems. HLT valve (Heart Leaflet Technologies Inc., Maple Grove, MN, USA); Colibri valve (Colibri Heart Valve, LLC, Broomfield, CO, USA); Trinity valve (Transcatheter Technologies GmbH, Regensburg, Germany); TRISKELE valve (University College London, London, UK); Biovalve (Biotronik AG, Bülach, Switzerland); Inovare® (Braile Biomedica, São José do Rio Preto, Brazil); MicroPort® (MicroPort Medical Group, Shanghai, China).*

an alternative valve is beneficial. In such cases, it is difficult to justify a suboptimal result simply because an alternative technology was not accessible. Herein, we detail clinical situations where specific TAVI devices may be beneficial.

Iliofemoral anatomy

Transfemoral vascular access for TAVI is considered to be the route of choice. This technique reduces morbidity and even mortality compared to transthoracic TAVI¹, and expedites patient functional recovery. The ratio of the outer diameter of the vascular access sheath to the femoral artery is the most powerful predictor of major vascular complications². The downsizing of delivery catheter dimensions of several THV systems has therefore increased the proportion of patients suitable for the transfemoral approach. The CoreValve® Evolut™ R (23, 26, 29 mm; Medtronic, Dublin, Ireland) and SAPIEN 3 (23, 26 mm; Edwards Lifesciences, Irvine, CA, USA) THVs can be implanted using 14 Fr InLine™

(Medtronic) or expandable-sheath technology, respectively. These low-profile systems can facilitate transfemoral TAVI in vessels as small as 5.5 mm (SAPIEN 3) or even 5.0 mm (Evolut R).

Aortic root anatomy

Most patients considered for TAVI undergo multimodal imaging assessment of the aortic root. Multislice computed tomography (MSCT) and/or three-dimensional echocardiography are the imaging modalities of choice (according to availability and local expertise) to evaluate the annular dimensions (diameters, area, perimeter) and unique anatomical features of each patient. A variety of adverse anatomical features may complicate THV implantation, and in such cases the availability of multiple TAVI technologies can facilitate procedural safety.

BORDERLINE SIZING

All THVs have specific manufacturer guidelines for valve sizing. Each device covers a range of annular sizes and, therefore, varying degrees of THV oversizing for an annular range. For example, a 26 mm CoreValve Evolut R is suitable for annular diameters between 20 and 23 mm and yields perimeter oversizing between 13 and 30%. Not infrequently therefore, clinicians encounter cases where the annular dimensions fall between two valve sizes for a specific THV system. In these “borderline” cases, there is an often difficult choice between accepting less oversizing and the risk of paravalvular leak (PVL), or opting for more oversizing and the risk of annular rupture. In such instances, the availability of both balloon-expandable and self-expanding TAVI systems can be of considerable benefit, as annular sizes considered borderline for balloon-expandable devices (e.g., SAPIEN XT; Edwards Lifesciences) are within a favourable range for a self-expanding THV (e.g., CoreValve; Medtronic Inc.). In a multicentre study including 615 TAVI recipients, Dvir et al demonstrated that significant oversizing with either the SAPIEN XT or CoreValve was associated with adverse outcomes, and suggested that more favourable outcomes could have been achieved in such cases by

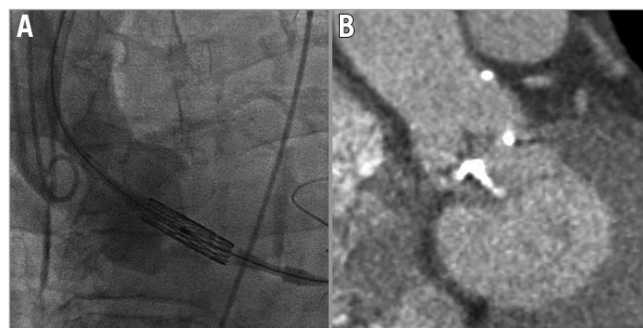


Figure 2. *Anatomical hurdles in TAVI. A) Left transcatheter implantation of the SAPIEN 3 valve in a vertical annulus facilitated by the deflectable Certitude delivery catheter. B) Left ventricular outflow tract calcification presenting a significant risk of annular rupture with a balloon-expandable system.*

switching to an alternative device³. These authors concluded that an individualised approach to device selection (not just device size) has the potential to improve outcome.

The introduction of the SAPIEN 3 valve, with the option to “undersize” the valve relative to the annulus or “overexpand” with extra contrast in the balloon, has reduced the frequency of truly borderline SAPIEN cases. Similarly, “undersizing” the THV has been more frequently observed with the Lotus™ valve (Boston Scientific Corporation, Marlborough, MA, USA).

CALCIUM QUANTIFICATION AND DISTRIBUTION

Left ventricular outflow tract (LVOT) calcification has been identified as the most important anatomic predictor of aortic root rupture during balloon-expandable TAVI⁴ (**Figure 2**). In such cases, physicians can opt to use a smaller THV size and risk greater PVL, or can remove contrast from the balloon to minimise the risk of rupture. An alternative solution is to use a self-expanding or mechanically expandable THV for these patients. While this strategy may indeed result in a greater risk of PVL, it avoids the potential for catastrophic aortic root rupture and appears to be gaining popularity worldwide.

AORTIC ROOT ANGULATION

Highly angulated aortic root anatomy (“vertical annulus” or “horizontal aorta”) can render THV implantation extremely challenging as coaxial implantation of the valve is compromised (**Figure 2**). Even when the aortic root is not excessively angulated, accurate implantation can be difficult due to the stiffness of the delivery system, tortuosity of the peripheral vasculature, or if right common carotid/right subclavian artery vascular access is used. Indeed, aortic root angulation $>30^\circ$ is considered to be a relative contraindication for CoreValve implantation via the right subclavian artery.

Non-coaxial valve deployment can result in valve embolisation, limited control of implantation depth, repeated valve resheathing and recapture, and the consequences of inaccurate deployment: moderate-severe PVL, new pacemaker implantation, mitral regurgitation, coronary occlusion, and requirement for a second valve. The availability of deflectable delivery catheters, such as the Edwards Certitude and Commander systems, and the ability to resheath and reposition the valve can greatly facilitate THV implantation, even in the most angulated anatomies.

CORONARY ARTERY OCCLUSION

Coronary artery occlusion is a rare but devastating complication of TAVI⁵ whose incidence has decreased since the advent of MSCT sizing and the recognition of anatomic risk factors: low height coronary ostia (<10 mm); narrow aortic sinuses (<2 mm diameter on either side of the THV); bulky and heavily calcified leaflets; and specific valve-in-valve procedures (e.g., Mitraflow and Freedom valves [Sorin Group, Milan, Italy]). Nevertheless, the availability of recapturable and repositionable TAVI systems should be considered in cases where the possibility of coronary occlusion is considered significant.

Bicuspid aortic valve

In patients with bicuspid aortic valve (BAV) stenosis, abnormal cusp fusion, asymmetry of the valve orifice and annulus, heavily calcified and fibrotic leaflets, and calcified raphe have the potential to yield suboptimal results with TAVI. Indeed, an early study of TAVI in BAV using first-generation devices reported a higher incidence of moderate PVL relative to tricuspid aortic valve stenosis⁶. Although MSCT imaging was sporadically applied in this nascent study (thereby making the results difficult to interpret), there is clearly a suggestion that BAV presents unique procedural challenges for TAVI. Overcoming these obstacles is of paramount importance as TAVI extends to younger patient cohorts with a higher prevalence of BAV morphology.

Recently, Perlman et al reported a multicentre experience of the SAPIEN 3 valve in 51 patients with BAV stenosis⁷. In this small series, there was no valve embolisation, no requirement for a second valve, and no patient had greater than mild PVL. The requirement for a new pacemaker was relatively high (23.5%), perhaps reflecting the proximity of the non-right commissure to the membranous septum.

It is also likely that the Lotus valve, Direct Flow valve (Direct Flow Medical, Santa Rosa, CA, USA), and repositionable self-expanding valves (Evolut R [Medtronic] and Portico [St. Jude Medical, St. Paul, MN, USA]) will overcome some of the limitations of the foundation THV devices in treating BAV anatomy. In particular, the ability to reposition the device and the presence of a sealing skirt or membrane appear central to improving results. It is also notable that in China, where up to 50% of all TAVI recipients have BAV, self-expanding devices with significantly enhanced radial force have been specifically developed to manage the greater burden of calcium seen in patients with BAV (e.g., MicroPort®; MicroPort Inc., Shanghai, China).

Accumulating experience with TAVI in BAV stenosis has led to the emerging concept of supra-annular sizing. This technique refers to the selection of a THV sized not to the annulus (annular sizing), but rather to the area of maximal calcification and minimal aortic root diameter. This usually occurs 2-4 mm cranial of the annulus, and is more frequently observed in BAV stenosis due to the presence of calcified raphe and more diffusely distributed calcium throughout the body of the leaflets than in trileaflet aortic valve stenosis. It has been acknowledged for some time that THVs do not just anchor and seal at annular level, but along the entire leaflet length. It is likely that supra-annular anchoring and sealing is occurring in many cases of alleged THV “undersizing”. “Undersizing” is therefore an unhelpful misnomer which should be avoided as it has the potential to create uncertainty regarding THV sizing.

Aortic regurgitation

Pure aortic regurgitation is perhaps the least studied application of THV technology. An early assessment of foundation devices in this setting suggested an increased requirement for valve-in-valve procedures (18.6%), a higher incidence of PVL (\geq grade 2: 21%), and

lower Valve Academic Research Consortium-defined success rates of 74.4%⁸. These suboptimal results relate to the absence of valvular calcification which impedes the ability of the THV to anchor, and perhaps instability of the prosthesis during deployment caused by the regurgitant jet. Interaction characteristics between the valve and anatomy differ between aortic stenosis and aortic regurgitation, and specific oversizing principles are required for non-calcified regurgitant valves (for self-expanding THV, >25% perimeter oversizing). Medical device companies and the interventional community must endeavour to develop this important information in the near future.

In September 2013, the JenaValve (JenaValve Technology GmbH, Munich, Germany) received CE-mark approval for the treatment of pure aortic regurgitation. This transapical system clips the native leaflets and does not rely on radial force for anchoring at the level of the aortic annulus. Results in a small multicentre study are encouraging but the requirement for transapical access has limited the adoption of this technology.

Several case reports have documented the use of repositionable devices in the setting of pure aortic regurgitation. Selection of these devices seems appropriate as they can be removed if suboptimal results are achieved.

Failing surgical aortic valves

The use of THV technology for the treatment of failing surgical aortic bioprostheses has greatly reduced the number of high-risk patients requiring redo surgical aortic valve replacement. All available THV systems have been successfully used in this setting, with universally acceptable results⁹. One exception, however, is in patients with small surgical bioprostheses (<21 mm). In such cases, the use of larger-than-necessary devices can lead to high transvalvular gradients (>20 mmHg), ongoing symptoms, and increased mortality. Therefore, while it remains feasible to implant any device in small anatomies, the best haemodynamic results can be expected when smaller devices or those with supra-annular leaflets are used. In the Valve-in-Valve International Data (VIVID) Registry, elevated post-procedural gradients were more common with balloon-expandable devices compared to self-expanding devices (HR 1.87, 95% CI: 1.21-2.9; p=0.005) for small and intermediate-sized surgical valves (41.2% vs. 23.4%, p=0.04; 35.8% vs. 19.4%, p=0.01, respectively)⁹. It is thus recommended that redo surgery be strongly considered in patients with internal surgical valve diameters <21 mm and that the 20 mm SAPIEN XT or 23 mm CoreValve Evolut R be used when redo surgery is not feasible. The ViV Aortic smartphone application provides an excellent resource for guiding device selection and implantation for these procedures.

One possible advantage of using repositionable (rather than balloon-expandable) technology in this setting is the potential to reduce the requirement for a second THV. In the VIVID Registry, a second device was implanted in 5.7% of patients (self-expanding 7.5% vs. balloon-expandable 4.1%; p=0.05)⁹. The option to recapture is also of particular relevance when the original surgical

prosthesis presents a high risk of coronary occlusion or when control of implantation depth may be challenging (e.g., severe aortic regurgitation).

Non-aortic valve intervention

THV technology has also been applied to mitral and tricuspid valve-in-valve or valve-in-ring procedures and to the treatment of dysfunctional right ventricle-to-pulmonary artery conduits. These procedures were initially performed exclusively with the SAPIEN XT valve but the Lotus and Direct Flow prostheses have been successfully used more recently for mitral interventions. Again, the ViV Mitral smartphone application provides guidance for these procedures. Self-expanding prostheses are not applicable for non-aortic valve interventions.

Conclusion

A variety of clinical scenarios exists where the availability of multiple transcatheter devices in a single institution may enhance individual patient outcomes. An individualised approach to TAVI device selection based on three-dimensional pre-procedural imaging is therefore advocated.

Conflict of interest statement

D. Mylotte, T. Modine and N. Piazza are consultants for Medtronic and MicroPort. M. Lee has no conflicts of interest to declare.

References

1. Blackstone EH, Suri RM, Rajeswaran J, Babaliaros V, Douglas PS, Fearon WF, Miller DC, Hahn RT, Kapadia S, Kirtane AJ, Kodali SK, Mack M, Szeto WY, Thourani VH, Tuzcu EM, Williams MR, Akin JJ, Leon MB, Svensson LG. Propensity-matched comparisons of clinical outcomes after transapical or transfemoral transcatheter aortic valve replacement: a placement of aortic transcatheter valves (PARTNER)-I trial sub-study. *Circulation*. 2015;131:1989-2000.
2. Hayashida K, Lefevre T, Chevalier B, Hovasse T, Romano M, Garot P, Mylotte D, Uribe J, Farge A, Donzeau-Gouge P, Bouvier E, Cormier B, Morice MC. Transfemoral aortic valve implantation new criteria to predict vascular complications. *JACC Cardiovasc Interv*. 2011;4:851-8.
3. Dvir D, Webb JG, Piazza N, Blanke P, Barbanti M, Bleiziffer S, Wood DA, Mylotte D, Wilson AB, Tan J, Stub D, Tamburino C, Lange R, Leipzig J. Multicenter evaluation of transcatheter aortic valve replacement using either SAPIEN XT or CoreValve: Degree of device oversizing by computed-tomography and clinical outcomes. *Catheter Cardiovasc Interv*. 2015;86:508-15.
4. Barbanti M, Yang TH, Rodes Cabau J, Tamburino C, Wood DA, Jilaihawi H, Blanke P, Makkar RR, Latib A, Colombo A, Tarantini G, Raju R, Binder RK, Nguyen G, Freeman M, Ribeiro HB, Kapadia S, Min J, Feuchtner G, Gurtvich R, Alqoofi F, Pelletier M, Ussia GP, Napodano M, de Brito FS Jr, Kodali S, Norgaard BL, Hansson NC, Pache G, Canovas SJ, Zhang H, Leon MB, Webb JG, Leipzig J. Anatomical and procedural features associated with aortic

root rupture during balloon-expandable transcatheter aortic valve replacement. *Circulation*. 2013;128:244-53.

5. Ribeiro HB, Webb JG, Makkar RR, Cohen MG, Kapadia SR, Kodali S, Tamburino C, Barbanti M, Chakravarty T, Jilaihawi H, Paradis JM, de Brito FS Jr, Canovas SJ, Cheema AN, de Jaegere PP, Del Valle R, Chiam PT, Moreno R, Pradas G, Ruel M, Salgado-Fernandez J, Sarmento-Leite R, Toeg HD, Velianou JL, Zajarias A, Babaliaros V, Cura F, Dager AE, Manoharan G, Lerakis S, Pichard AD, Radhakrishnan S, Perin MA, Dumont E, Larose E, Pasian SG, Nombela-Franco L, Urena M, Tuzcu EM, Leon MB, Amat-Santos IJ, Leipsic J, Rodes-Cabau J. Predictive factors, management, and clinical outcomes of coronary obstruction following transcatheter aortic valve implantation: insights from a large multicenter registry. *J Am Coll Cardiol*. 2013;62:1552-62.

6. Mylotte D, Lefevre T, Sondergaard L, Watanabe Y, Modine T, Dvir D, Bosmans J, Tchetché D, Kornowski R, Sinning JM, Theriault-Lauzier P, O'Sullivan CJ, Barbanti M, Debry N, Buithieu J, Codner P, Dorfmeister M, Martucci G, Nickenig G, Wenaweser P, Tamburino C, Grube E, Webb JG, Windecker S, Lange R, Piazza N. Transcatheter aortic valve replacement in bicuspid aortic valve disease. *J Am Coll Cardiol*. 2014;64:2330-9.

7. Perlman GY, Blanke P, Dvir D, Pache G, Modine T, Barbanti M, Holy EW, Treede H, Ruile P, Neumann FJ, Gandolfo C, Saia F, Tamburino C, Mak G, Thompson C, Wood D, Leipsic J, Webb JG. Bicuspid Aortic Valve Stenosis: Favorable Early Outcomes With a Next-Generation Transcatheter Heart Valve in a Multicenter Study. *JACC Cardiovasc Interv*. 2016;9:817-24.

8. Roy DA, Schaefer U, Guetta V, Hildick-Smith D, Mollmann H, Dumonteil N, Modine T, Bosmans J, Petronio AS, Moat N, Linke A, Moris C, Champagnac D, Parma R, Ochala A, Medvedofsky D, Patterson T, Woitek F, Jahangiri M, Laborde JC, Brecker SJ. Transcatheter aortic valve implantation for pure severe native aortic valve regurgitation. *J Am Coll Cardiol*. 2013;61:1577-84.

9. Dvir D, Webb JG, Bleiziffer S, Pasic M, Waksman R, Kodali S, Barbanti M, Latib A, Schaefer U, Rodes-Cabau J, Treede H, Piazza N, Hildick-Smith D, Himbert D, Walther T, Hengstenberg C, Nissen H, Bekeredjian R, Presbitero P, Ferrari E, Segev A, de Weger A, Windecker S, Moat NE, Napodano M, Wilbring M, Cerillo AG, Brecker S, Tchetché D, Lefevre T, De Marco F, Fiorina C, Petronio AS, Teles RC, Testa L, Laborde JC, Leon MB, Kornowski R. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. *JAMA*. 2014;312:162-70.