New paradigms for the sequential treatment of severe aortic stenosis: imaging-guided selection of the first intervention paves the way for lifetime management

Bernard D. Prendergast[1,2]*, DM, FRCP; Tiffany Patterson[1], PhD, FRCP

1. St Thomas' Hospital, London, United Kingdom; 2. Cleveland Clinic London, London, United Kingdom

Not so long ago, towards the end of the last century, surgical aortic valve replacement (SAVR) with a mechanical prosthesis combined with lifelong anticoagulation using vitamin K antagonists (requiring regular haematological monitoring and with an attendant risk of bleeding) was the only treatment option for patients with severe aortic stenosis. The mainstream application of bioprosthetic surgical valves in the 1980s and 1990s presented a major breakthrough, allowing older patients at higher risk of bleeding the possibility of surgery without the need for lifelong anticoagulation. These patients were initially deemed unlikely to outlive their valve and the prospect of a second intervention was seldom considered.

Fast forward three decades and bioprosthetic valves are now used in the vast majority of patients undergoing aortic valve surgery while transcatheter aortic valve implantation (TAVI) has established its safety and efficacy across the spectrum of surgical risk such that clinical and anatomical factors (including age and life expectancy) now drive the choice between TAVI and SAVR[1,2]. In 2022, no one wants a mechanical valve and bioprosthetic valves are used in the majority of patients aged greater than 50 years undergoing surgery (driven by their reduction in bleeding complications, lower risk of valve thrombosis, and patient preference), often without robust evidence to support their durability.

Meanwhile, TAVI is rapidly supplanting SAVR as the gold standard for first-time intervention for aortic stenosis, and valve-in-valve TAVI is a commonplace intervention for patients with failing surgical bioprostheses.

These seismic developments have transformed the management of patients with aortic stenosis and generated a new conversation concerning their lifetime journey, entailing a need for appropriate planning and optimal sequencing in the context of repeated valve interventions. The notion that successive TAVI (so-called TAV-in-TAV or revalving) procedures[3] can be undertaken every ten years or so throughout a patient's lifetime is appealing but overly simplistic for several reasons. First, the long-term durability of current TAVI devices remains unknown. Although data from the randomised trials and international registries are reassuring out to eight years, it will be some time before ten- to fifteen-year data become available to match those of contemporary surgical bioprosthetic valves[4]. Second, many younger patients with aortic stenosis have bicuspid valves – a population that was excluded from the pivotal randomised TAVI trials. Although registry data have demonstrated positive outcomes in carefully selected patients with bicuspid valves undergoing TAVI in highly experienced centres[5], there is much to learn with regard to optimal device sizing

---

Corresponding author: Cleveland Clinic London, 33 Grosvenor Place, London, SW1X 7HY, United Kingdom.
E-mail: PRENDEB2@ccf.org

and procedural technique[6]. Third, successive device implants may be the cause of progressive patient-prosthesis mismatch, which is associated with increased mortality and morbidity in both SAVR and TAVI recipients[7]. Fourth, multiple overlapping transcatheter heart valve frames in the aortic root (particularly those of supra-annular design) may present technical challenges at the time of diagnostic coronary angiography or percutaneous coronary intervention in individuals with pre-existing or *de novo* coronary artery disease (and could also be associated with a heightened risk of valve or coronary thrombosis over prolonged follow-up). And finally, if needed, surgical excision of TAVI devices is frequently difficult, with an increased incidence of adverse outcomes and high likelihood of aortic wall injury[8].

A more sophisticated approach involving careful forethought, consideration of different interventional sequences and meticulous procedural planning is therefore essential when mapping out the lifetime journey of patients with aortic stenosis. In this issue of EuroIntervention, Medranda et al[9] present a novel study utilising computed tomography (CT) simulation techniques to determine the risks of coronary obstruction (a potentially fatal complication of TAVI) in subjects undergoing a virtual TAV-in-TAV procedure. Amongst 213 participants enrolled in the low-risk TAVI (LRT) trial and EPROMPT registry, the accuracy of CT modelling was confirmed by a high level of concordance between predicted valve-to-coronary distance at baseline and 30-day follow-up. Subsequent CT simulation of TAVI followed by redo TAV-in-TAV predicted a low risk of coronary obstruction in 25% of subjects and a high risk in 28% (owing to sinus sequestration with need for leaflet modification or TAVI explant), regardless of the type of implanted valve. Redo TAV-in-TAV in the remaining 47% was associated with a low risk of coronary obstruction when using a balloon-expandable valve but a substantially higher risk when using a self-expanding valve. Within the constraints of CT modelling algorithms (and notwithstanding the numerous other clinical and anatomical factors outlined above), these findings demonstrate

considerable interindividual variation in the feasibility of repeated TAV-in-TAV procedures, the potential importance of modified implantation techniques (such as commissural alignment) in at-risk subjects (particularly when using self-expanding valves), a need for continued bioengineering advances in this field, the importance of detailed imaging analysis in determining the appropriate choice of transcatheter heart valve and sequence of interventional procedures, and the potential role of CT simulation in guiding the lifetime journey for patients with aortic stenosis.

Surgical and transcatheter interventions are complementary options for patients with valve disease, and the pros and cons of different procedural sequences over the lifetime journey of patients with aortic stenosis is now a hot topic **(Figure 1)**[10]. Whilst the appropriate treatment algorithm may be self-evident for patients in their seventh or eighth decades, careful consideration is essential in younger patients who may face the prospect of three or four interventions – particularly those with grown-up congenital heart disease (who may have already undergone surgery or transcatheter intervention in infancy or childhood) and women of childbearing age who may wish to avoid the hazards of mechanical valves and mandated anticoagulation during pregnancy.

The present data reaffirm that the first intervention paves the way for lifetime management of patients with aortic stenosis. As in all aspects of TAVI, careful CT-facilitated preprocedural planning and a multidisciplinary Heart Team discussion concerning specific clinical and anatomical factors are essential to achieve the optimal lifelong outcome for individual patients.

Conflict of interest statement

B. Prendergast reports research and education grants to the institution from Edwards Lifesciences; consultancy fees from Microport and Anteris; speaker fees from Abbott, Medtronic and Edwards Lifesciences; and participation on the Colibri Data Safety Monitoring Board. T. Patterson has no conflicts of interest to declare.

SAVR-TAVI-TAVI		TAVI-SAVR-TAVI		TAVI-TAVI-TAVI	
Benefit	**Risk**	**Benefit**	**Risk**	**Benefit**	**Risk**
TAVI-in-SAVR well established	Limited options for 4th procedure	4th procedure feasible	Experience of TAVI explantation remains limited	Minimally invasive procedure at young age	High risk of coronary obstruction at the time of TAV-in-TAV
Ease of coronary access after SAVR	Difficult coronary access after TAVI-in-SAVR	TAVI-in-SAVR feasible as a 3rd procedure	Need for concomitant aortic wall repair		Potentially challenging coronary access
SAVR at young age	High risk of coronary obstruction at the time of TAV-in-TAV	Minimally invasive procedure at young age			Feasible in limited number of patients

Figure 1. *Risks and benefits of three potential interventional sequences in the lifetime management of severe aortic stenosis. Adapted with permission from reference 10. SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation*

References

1. Siontis GCM, Overtchouk P, Cahill TJ, Modine T, Prendergast B, Praz F, Pilgrim T, Petrinic T, Nikolakopoulou A, Salanti G, Sondergaard L, Verma S, Juni P, Windecker S. Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: an updated meta-analysis. *Eur Heart J.* 2019;40:3143-53.

2. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, Capodanno D, Conradi L, De Bonis M, De Paulis R, Delgado V, Freemantle N, Haugaa KH, Jeppsson A, Jüni P, Pierard L, Prendergast BD, Sadaba JR, Tribouilloy C, Wojakowski W. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *EuroIntervention.* 2022;17:e1126-96.

3. Landes U, Webb JG, De Backer O, Sondergaard L, Abdel-Wahab M, Crusius L, Kim WK, Hamm C, Buzzatti N, Montorfano M, Ludwig S, Schofer N, Voigtlaender L, Guerrero M, El Sabbagh A, Rodes-Cabau J, Guimaraes L, Kornowski R, Codner P, Okuno T, Pilgrim T, Fiorina C, Colombo A, Mangieri A, Eltchaninoff H, Nombela-Franco L, Van Wiechen MPH, Van Mieghem NM, Tchetche D, Schoels WH, Kullmer M, Tamburino C, Sinning JM, Al-Kassou B, Perlman GY, Danenberg H, Ielasi A, Fraccaro C, Tarantini G, De Marco F, Witberg G, Redwood SR, Lisko JC, Babaliaros VC, Laine M, Nerla R, Castriota F, Finkelstein A, Loewenstein I, Eitan A, Jaffe R, Ruile P, Neumann FJ, Piazza N, Alosaimi H, Sievert H, Sievert K, Russo M, Andreas M, Bunc M, Latib A, Govdfrey R, Hildick-Smith D, Sathananthan J, Hensey M, Alkhodair A, Blanke P, Leipsic J, Wood DA, Nazif TM, Kodali S, Leon MB, Barbanti M. Repeat transcatheter aortic valve replacement for transcatheter prosthesis dysfunction. *J Am Coll Cardiol.* 2020;75:1882-93.

4. Arsalan M, Walther T. Durability of prostheses for transcatheter aortic valve implantation. *Nat Rev Cardiol.* 2016;13:360-7.

5. Makkar RR, Yoon SH, Leon MB, Chakravarty T, Rinaldi M, Shah PB, Skipper ER, Thourani VH, Babaliaros V, Cheng W, Trento A, Vemulapalli S, Kapadia SR, Kodali S, Mack MJ, Tang GHL, Kaneko T. Association Between Transcatheter Aortic Valve Replacement for Bicuspid vs Tricuspid Aortic Stenosis and Mortality or Stroke. *JAMA.* 2019;321:2193-202.

6. Xiong TY, Ali WB, Feng Y, Hayashida K, Jilaihawi H, Latib A, Lee MK, Leon MB, Makkar RR, Modine T, Naber C, Peng Y, Piazza N, Reardon MJ, Redwood S, Seth A, Sondergaard L, Tay E, Tchetche D, Yin WH, Chen M, Prendergast B, Mylotte D. Transcatheter aortic valve replacement in patients with bicuspid valve morphology: a roadmap towards standardization. *Nat Rev Cardiol.* 2022 Jun 20. [Epub ahead of print].

7. Herrmann HC, Daneshvar SA, Fonarow GC, Stebbins A, Vemulapalli S, Desai ND, Malenka DJ, Thourani VH, Rymer J, Kosinski AS. Prosthesis-Patient Mismatch in Patients Undergoing Transcatheter Aortic Valve Replacement: From the STS/ACC TVT Registry. *J Am Coll Cardiol.* 2018;72:2701-11.

8. Bapat VN, Zaid S, Fukuhara S, Saha S, Vitanova K, Kiefer P, Squiers JJ, Voisine P, Pirelli L, von Ballmoos MW, Chu MWA, Rodés-Cabau J, DiMaio JM, Borger MA, Lange R, Hagl C, Denti P, Modine T, Kaneko T, Tang GHL; EXPLANT-TAVR Investigators. Surgical Explantation After TAVR Failure: Mid-Term Outcomes From the EXPLANT-TAVR International Registry. *JACC Cardiovasc Interv.* 2021;14:1978-91.

9. Medranda GA, Soria Jimenez CE, Torguson R, Case BC, Forrestal BJ, Ali SW, Shea C, Zhang C, Wang JC, Gordon P, Ehsan A, Wilson SR, Levitt R, Parikh P, Bilfinger T, Hanna N, Buchbinder M, Asch FM, Weissman G, Shults CC, Garcia-Garcia HM, Ben-Dor I, Satler LF, Waksman R, Rogers T. Lifetime management of patients with symptomatic severe aortic stenosis: a computed tomography simulation study. *EuroIntervention.* 2022;18:e407-16.

10. Yerasi C, Rogers T, Forrestal BJ, Case BC, Khan JM, Ben-Dor I, Satler LF, Garcia-Garcia HM, Cohen JE, Kitahara H, Shults C, Waksman R. Transcatheter Versus Surgical Aortic Valve Replacement in Young, Low-Risk Patients With Severe Aortic Stenosis. *JACC Cardiovasc Interv.* 2021;14:1169-80.