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EDITORIAL COMMENT

TAV-in-TAV and Beyond

How Far Can We Go?*

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Whether by an open surgical approach or, more recently, through percutaneous access, replacement of the aortic valve (AV) has become commonplace in clinical practice. Although it was still in 1512 that Leonardo da Vinci recognized the central nature of the AV with its swirling eddies within sinuses,[1] it was only 4 centuries later that Theodore Tuffier,[2] in 1912, performed the first closed AV intervention using his own finger to free the fused leaflets of a stenosed valve. In 1952, Charles Hufnagel[3] implanted a heterotopic heart valve prosthesis in the descending aorta of a patient with AV regurgitation, and in 1960, Dwight Harken[4] performed the first implant of a "double-caged ball" prosthesis in the annular position.

The pathway for the development of catheter-based AV interventions began to be paved in 1965 when Alain Cribier performed the first balloon aortic valvuloplasty.[5] Although this approach emerged as an alternative for patients with symptomatic severe AV stenosis in cardiogenic shock or for symptom palliation in those considered too frail for conventional surgical AV replacement, its long-term outcomes were considered poor.[5]

Following in the footsteps of the development of balloon-expandable (BE) coronary artery stenting, Henning Rud Andersen[6] developed a porcine BE AV stent, which he successfully implanted in a porcine model in 1992. Anticipating that the transcatheter treatment of the AV would be a "breakthrough lifesaving treatment for hundreds of thousands of patients with AV stenosis," he formulated 5 requirements for implanting heart valves percutaneously, which have remained valid until today (**Figure 1**).

Ten years after Andersen's groundbreaking experiment, Alain Cribier performed the first transcatheter AV implantation (TAVI) on April 16, 2002. The patient was a 57-year-old man with severe calcific AV stenosis, and peripheral vascular disease with a previous aorto-bifemoral bypass, who presented in cardiogenic shock. The percutaneous heart valve was crimped onto a 30-mm balloon and advanced through a 24-F sheath inserted into the right femoral vein. Using antegrade transseptal access and establishing a venous-arterial loop, the atrial septum and mitral valve were crossed and the prosthetic valve was advanced, positioned, and deployed into the native aortic annulus using rapid balloon inflation and deflation. Despite intense skepticism faced by Cribier, this successful procedure marked the beginning of a revolution in interventional cardiology.[7]

Some years later Eberhard Grube, in 2005, deployed a new self-expandable device, the CoreValve™, in an inoperable 73-year-old woman with severe symptomatic AV stenosis. A retrograde approach via the common iliac artery was used for the valve deployment and the contralateral femoral artery was used for temporary extracorporeal circulation, unloading the left ventricle during the stent expansion.[8] In 2006, Webb et al[9] published a series of 15 successful valve implants through a retrograde femoral artery approach, using 22- and 24-F sheaths. He argued that the femoral transarterial, retrograde approach was more intuitive and more generalizable.

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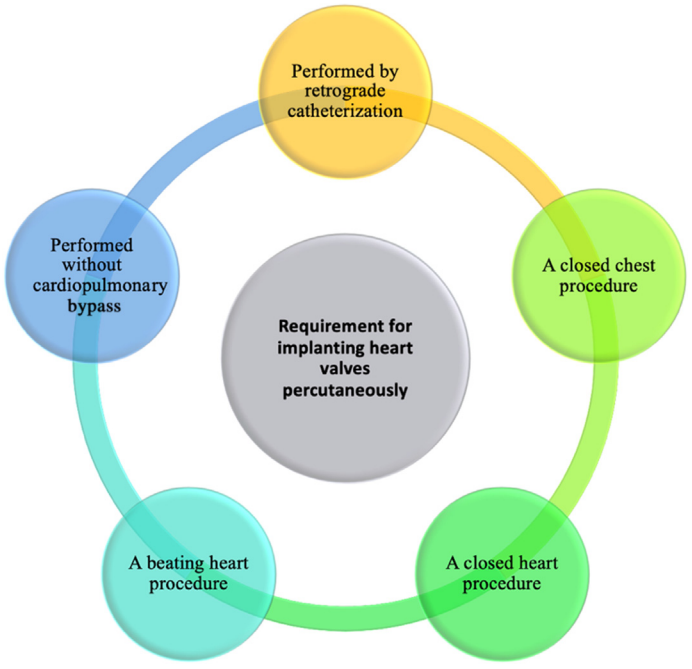
FIGURE 1 Requirement for THV Implantation



Requirement for implanting heart valves percutaneously according to Andersen.[6]
THV = transcatheter heart valve.

This was the beginning of what has become the first-line and most common access route for TAVI.[9]

Since these first-in-human procedures, the interest of the scientific community in AV transcatheter treatment has grown exponentially, making it the most studied and intervened-upon heart valve. Today the implant of a transcatheter heart valve (THV) has become the first-line treatment in high-risk, inoperable patients with severe AV stenosis and has been proven equivalent in those patients at intermediate and low surgical risk.[10,11] However, regardless of the undeniable progress that TAVI technology has achieved, including improvements in implantation techniques and operator skills, there are still some important concerns regarding this method. One of the most relevant current concerns is the expansion to younger and healthier patients who are expected to outlive their initial bioprosthesis. How durable are these valves? In this scenario, the focus of the AV interventions must now shift from the first to the subsequent procedures, regardless of whether the index intervention was an open or a percutaneous valve implantation.[12]

In this issue of *JACC: Case Reports*, Hatab et al[13] described a case of a patient with 3 previous surgical AV replacements, the last being a homograft. This was followed by a TAV-in homograft that now requires a TAV-in-TAV-in homograft due to severe AV regurgitation manifesting as cardiogenic shock. The patient's surgical history began in his 20s secondary to rheumatic disease. The 2 first open surgeries were mechanical AV replacements and the last one a homograft for treatment of infective endocarditis. This was followed by a 34-mm Evolut R implant in the homograft, and then a 34-mm Evolut FX (Medtronic) in the former Evolut R.[13]

Despite his previous cardiac interventions, the patient's Society of Thoracic Surgeons (STS) score was still classified as "low risk" (STS predicted risk of mortality: 2.4%) probably due to his young age (59 years). This is not so uncommon in our daily clinical practice and alerts us to the fact that there are some high-risk situations, such as re-sternotomy with patent coronary artery grafts, which are not accurately accounted for by the current surgical risk scores.

Furthermore, we can use this case to exemplify the importance of patient lifetime management. A decision to implant a THV in a young patient with AV disease, requires the recognition that the patient will probably need a second, and maybe a third valve during their lifetime. The way we perform the first intervention and the device we choose will be crucial for the subsequent procedures' feasibility and success.

Nowadays, interventions in degenerated THV include TAVI surgical explantation or redo-TAVI (TAV-in-TAV). This decision is based on several factors, such as the patient's clinical status, the patient's goals and preferences, the cause of valve failure, aortic root and coronary artery anatomy, and the geometric features of the index THV. Although TAVI explantation is probably the mainstay therapy in THV endocarditis, valve thrombosis, significant paravalvular leakage, or prosthesis-patient mismatch, or in the case of prohibitive risk of coronary occlusion, redo-TAVI seems to be a less invasive and less morbid procedure, especially for patients with high surgical risk.[14]

In a comparison of TAVI explantation with redo-TAVI, the EXPLANTORREDO-TAVR International Registry showed that redo-TAVI had a significantly lower 30-day (3.4% vs 13.6%; $P < 0.001$) and 1-year (15.4% vs 32.4%; $P = 0.001$) mortality rate, driven mainly by the early TAVI explantation hazard. Importantly, there was no difference in the reintervention strategy regardless of the index THV (BE vs self-expandable device), although BE failure was preferentially treated using non-BE devices, and non-BE valve failure was preferentially treated with BE device. In the TAVI explantation group, failure of non-BE devices required a higher proportion of

TABLE 1 TAV-in-TAV Preprocedural Planning Guide According to Tarantini et al[18]

Analyze the pre-index TAVI CT (if available)	• Evaluate the native aortic root (bicuspid or tricuspid valve morphology, eccentricity, calcium distribution, annular and LVOT dimensions)
Evaluate the anatomic position of the index THV	• Implant height • Valve position in relation to the annulus plane • Degree of the index THV expansion • Coronary ostia commissural alignment • Distance of the coronary ostia in relation to the stent frame and leaflets • Native annulus and LVOT dimensions • Degree and distribution of native valve calcification • Sinotubular junction size and height
Evaluate the index THV dimensions	• Valve type and size (the actual index THV dimensions in a specific patient anatomy may differ from those described in technical sizing charts)
Consider the technical design specific of each THV available	• Stent frame height, stent cell form and size, stent expansion • Degree and form of stent expansion • Commissural stent post height • Valve position (supra- vs intra-annular) • Skirt length
Analyze the pre-redo TAVI CT	• Confirm that the index THV implanted type corresponds with the one specified • Evaluate the mode of the index THV failure (hypo-attenuating leaflet thickening, pannus, leaflet calcification, PVL, or central regurgitation) • Understand the percentage of oversizing/undersizing of the index THV • Measure minimum and maximum internal diameter, eccentricity, area-derived internal diameter, and perimeter-derived internal diameter • Evaluate the aortic root anatomy • Access the position of the index THV in relation to its surrounding structures • Estimate the risk of coronary obstruction, sinus sequestration, and difficult coronary access • Estimate the risk of prosthesis-patient mismatch and residual PVL • Anticipated the degree of leaflet overhang

CT = computed tomography; LVOT = left ventricular outflow tract; PVL = paravalvular leak; TAVI = transcatheter aortic valve implantation; THV = transcatheter heart valve.

concomitant root replacement (13.9% vs 5.6%; $P = 0.087$). This registry also observed that, in general, the rate of need for TAVI reintervention rate was <1%, but with an increasing trend during the most recent period of the study.[15]

These data add to previous reports that have suggested the safety of the TAV-in-TAV procedure with a similar 30-day (4.9% vs 4.1%; $P = 0.47$) and 1-year mortality (15.6% vs 18.6%; $P = 0.33$) rate compared with native TAVI, even in an elderly (78.5 ± 9.7 years vs 78.6 ± 9.7 years) and high-risk patient population (STS score 8.9% ± 7.7% vs 8.6% ± 9.3%).[16] On the other hand, surgical TAVI explantation has been associated with a non-neglectable early mortality of near 30% at 1 year (30-day: 13.1%; 1-year: 28.5%).[17]

In light of these findings, one can speculate that redo-TAVI will likely become the treatment of choice for THV failure. However, there is still a lack of clear evidence on how this procedure should be planned and performed, its potential risks, and how to prevent them. To mitigate the risks of a redo-TAVI, broad and accurate preprocedural planning and a deep knowledge of the THV features is of paramount importance. A guide on the main features to be evaluated during a preprocedural TAV-in-TAV planning was recently presented by Tarantini et al[18] and it is summarized in **Table 1**.

In conclusion, although TAVI has undoubtedly been a disruptive technology that has transformed the modern treatment of AV stenosis, new improvements and solutions to address the still-existing challenges are necessary to achieve a safer and successful lifetime treatment of AV disease. Focusing on the first TAVI procedure is not enough. To push the TAVI limits, expanding its indication to TAV-in-TAV and beyond, a thorough understanding of lifetime management with a patient-tailored approach must be pursued, foreseeing the likelihood of further intervention.

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