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Letter to the Editor

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A Precipitous Decision: Transcatheter Aortic Valve Replacement in Low-Risk Patients

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To the Editor

Long before US Food and Drug Administration (FDA) approval of transcatheter aortic valve replacement (TAVR) for low and intermediate surgical risk patients with aortic stenosis, the exercise of Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) estimation and discussion of the modality of aortic valve replacement (AVR) were becoming increasingly redundant. This was mainly driven by the increasing simplicity of the ever-developing TAVR procedure and the patients' desire to avoid sternotomy. The clinicians' favored minimalist approach is exemplified by a report from real-world practice [1], where "heart teams" designated high or extremely high risk for surgical AVR (SAVR) in 91% of patients who underwent TAVR between January 2012 and June 2017; the corresponding STS-PROM score was < 3-8% in 71.6% of those patients. Although factors like porcelain aorta, hostile mediastinum, or previous coronary artery bypass graft (CABG) with a graft close to the sternum may have been considered, extreme discordance between estimated STS-PROM and heart-team designated risk for SAVR was evident.

In France tendency to treat lower-risk patients, with a reduction in median logistic EuroSCORE from 20.3% (interquartile range, 12.1-30.8%) to 13.6% (interquartile range, 9-21%), was reported between 2010 - 2015 [2].

After trials in intermediate and low surgical risk patients with aortic stenosis showed that TAVR was non-inferior to SAVR, "indication creep" for TAVR has led to ongoing trials to assert "prophylactic TAVR" in asymptomatic patients with severe aortic stenosis or in moderate aortic stenosis with heart failure or ventricular systolic dysfunction. Until recently, surgical risks and prosthesis-related complications acted as deterrent to valve replacement for "asymptomatic" patients with severe aortic stenosis reported on echocardiography. Instead extensive clinical effort was expended to determine optimal time for valve replacement. Very soon this will become inessential as well. A paradigm shift in the management of aortic stenosis appears to be on the horizon.

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The jeopardy of many under-studied complications and unknown long-term outcomes of the TAVR procedure and prosthesis is being overlooked amidst enthusiasm to avoid a sternotomy and cardiopulmonary bypass.

Uncertain durability

The long-term durability of conventional, surgically implantable bio-prosthesis has always been a concern; however, now, due to its unique delivery and implantation process, the accelerated structural valve degeneration of a TAVR prosthesis is dreaded even more. The leaflets and frame of the TAVR prosthesis must be "crimped" to allow percutaneous delivery over a catheter; this has been reported to cause altered collagen and microscopic damage, as observed by an electron microscope [3]. The effect of crimping is further accentuated by post-dilatation for secured placement. The long-term clinical effect of crimping has not been adequately explored. Potentially, areas of altered collagen may predispose thrombus formation and accelerated calcification. More thromboses have been reported for TAVR prostheses (up to 15%) compared to SAVR in the immediate post-procedure period [4].

Non-removal of annular calcium with TAVR (routinely done in all SAVR procedures) may lead to various degrees of asymmetric expansion of the TAVR valve frame. This may cause adverse leaflet-stent interaction and greater elliptical eccentricity, which if increased to 0.68, has been shown to increase the stress on leaflets by 143% and cause more aortic regurgitation (AR) due to coaptation abnormality [5]. Likewise, the oversizing of TAVR frames to minimize AR leads to under-expansion of the TAVR frame and increased mechanical stress.

TAVR prosthesis leaflets are usually thinner than those for SAVR. In a biomechanical experiment [6] examining leaflet fatigue due to cyclic loading, investigated using finite element analysis, TAVR prosthesis leaflets sustained higher stresses and strain and fatigue damage compared to SAVR prosthesis. Simulation results calculated the durability of a TAVR prosthesis as close to only 7.8 years [6].

How these laboratories generated qualitative insights into TAVR valve durability will pan out in real-world practice over time is not yet adequately known. Experience with Ionescu-Shiley bio-prosthesis indicates that despite normal functioning for 5 years, accelerated degeneration may start between 5 and 10 years [7]. Dr. Diver reported 18% and 50% degeneration of

TAVR prostheses at 6 and 8 years [8].

Undependable, deficient data for durability

Assessing long-term durability based on TAVR trials is confounded by many factors, including scant data beyond 5 years, progressive attrition of the sample size of earlier trials due to deaths, the non-standardized definition of structural valve deterioration, and the questionable accuracy of echocardiography data reported to various TAVR registries.

These limitations are apparent from the reports of excellent durability of TAVR prosthesis such as UK Transcatheter Aortic Valve Implantation (TAVI) registry [9] based on only 15.8% of the total number patients who underwent TAVR during the study period (2007 - 2011). Six-year report of the outcome of TAVR prosthesis in Nordic Aortic Valve Intervention (NOTION) trial [10] was confounded by the inclusion of patient-prosthesis mismatch (PPM) for the assessment of durability, when there was severe problem with the undersizing of the prosthesis in entire cohort, more so in the SAVR group.

Potential for disproportionate long-term harms in younger patients

Even more concerning is the unknown magnitude of neurological damage that occurs during TAVR. Non-removal of annular calcium and forceful dilatation of the stenotic valve cause the embolization of the calcium. Despite SENTINEL trial [11] reported that a protective device captured embolic debris in 99% of patients, clinical neurological deficits in 30 days post-procedure period have been reported in only 0.5-0.6% of patients in TAVR trials in low-risk patients [12, 13]. The consequences of "silent infarcts" reported as new defects in cerebral magnetic resonance imaging (MRI) in 84% of patients undergoing TAVR (much higher than SAVR) [14] remain unknown. The Rotterdam Scan Study [15] showed a doubled risk of dementia and serious cognitive decline in the presence of silent infarcts in diffusion-weighted MRI. Accepting heightened risk of dementia associated with TAVR in order to avoid sternotomy in low to intermediate surgical risk younger patients is short sighted.

Newer iterations of valve systems intended to minimize paravalvular AR (the Achilles' heel of the TAVR procedure) appear to result in more direct conduction-system trauma, resulting in the need for pacemaker placement and left bundle branch block (LBBB). The magnitude of conduction abnormality during TAVR is unclear due to the non-uniform reporting of both LBBB and pacemaker requirements across all studies. Recent trials indicated that up to 19.4% of patients required pacemakers after Evolut R TAVR [13], while 23.7% developed LBBB after Sapien Valve system [12]. The causative roles of LBBB and pacemakers (from right ventricular pacing and tricuspid regurgitation) in the development of heart failure and dilated cardiomyopathy are well known.

Management of coronary artery disease in patients undergoing TAVR

An effective management strategy for coronary artery disease (present in up to 65% of patients 80 years or older) in patients undergoing TAVR has never been explored. Patients with complex coronary disease (SYNTAX score of more than 22) and unprotected left main disease were excluded from the trials. In low- or intermediate-risk TAVR trials, the requirement for percutaneous transluminal coronary angioplasty (PTCA) was reported as only 3.9-14.5%. The feasibility and technical challenges of staged interventions and TAVR followed by percutaneous coronary intervention (PCI) have not been investigated in any large randomized trial. However, low complete revascularization rates (20-36.6%) have been reported in TAVR patients undergoing concomitant PCI [16]. Long-term outcomes regarding ventricular remodeling, symptom improvement and quality of life in cases of suboptimal revascularization remain unknown.

TAVR V/S emerging surgical options: Ozaki procedure

A head-to-head randomized trial comparing TAVR and new emerging surgical options, such as the Ozaki procedure or SAVR with a minimally invasive approach, mini-sternotomy (MIS), and right anterior thoracotomy (RAT), should have been considered before the approval of TAVR in younger patients who are otherwise excellent candidates for SAVR. The reconstruction of aortic valves from autologous pericardium (Ozaki procedure) not only obviates the need for a prosthesis but also overcomes the technical difficulties of AVR in patients with either small aortic annular diameter (20.3 ± 3.2 mm) or bicuspid aortic valve and even in patients with significant AR [17]. In addition, the Ozaki procedure can be undertaken concomitantly with CABG, mitral valve replacement (MVR), and Tricuspid valve replacement (TVR) [17, 18]. The durability of reconstructed valve is expected much longer than the bio-prosthesis made up of bovine pericardium [19]. Less late calcification was reported for autologous pericardial valve. The re-operation free survival was reported to be 47% at 16 years for autologous pericardial valve in one report while another report showed 100% freedom from SVD at 6.5 years of follow-up [20].

Potential of intervention bias associated with mushrooming TAVR centers

The precipitous action of the FDA has already added to the mushrooming, unmonitored growth of TAVR centers. This poses a real danger of an "intervention bias" of the self-interest type. TAVR may be performed for soft indications and with suboptimal results particularly in vulnerable populations such as octo/nonagenarians (who have many comorbidities and vague symptoms but an echocardiography criterion of severe aortic stenosis, as per current cardiology society guidelines), who may receive TAVR without an evaluation of the utility/futility of the procedure.

Cost-effectiveness estimates of TAVR: are they accurate?

One cannot overlook the extra cost associated with the TAVR procedure. Cost-effectiveness analyses have tried to justify a TAVR prostheses cost 5 - 6 times higher than that of a SAVR prosthesis assuming a lower long-term cost, which appears unreliable given that the future of TAVR prostheses remains unknown beyond the short term. These analyses are also inherently flawed because they are based on recent trial data for death, stroke, intensive care unit stay, and re-hospitalization and compare mostly isolated TAVR procedures to SAVR procedures in which 25-30% of patients also underwent concomitant procedures, significantly affecting all the above events.

Conclusions

Unanswered questions about TAVR need to be addressed through industry-independent trials before TAVR can be considered the preferred AVR modality in patients with aortic stenosis, who are otherwise excellent candidates for SAVR. A head-to-head comparison between TAVR and new emerging surgical options such as Ozaki procedure should be considered, since a reconstructed autologous valve appears much better option than a TAVR prosthesis.

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Conflict of Interest

None to declare.

Informed Consent

Not applicable.

Data Availability

The author declares that data supporting the findings of this study are available within the article.

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