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Review Article

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Aortic Stenosis and Transcatheter Aortic Valve Implantation: Current Status and Future Directions in Korea

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ABSTRACT

Transcatheter aortic valve implantation (TAVI) has been accepted as one of primary options for treatment of symptomatic severe aortic stenosis. Although TAVI has been predominantly used for patients at high risk or with old age who were not considered optimal candidates for surgical aortic valve replacement (SAVR), its indication is now expanding toward low risk profile and younger age. Many clinical trials are now ongoing to test the possibility of TAVI for use in patients even with uncharted indications who are not eligible for SAVR in current guidelines but may benefit from valve replacement. Current issues including periprocedural safety, long-term adverse events, hemodynamics and durability associated with TAVI should be also solved for expanding use of TAVI. The review presents current status and future directions of TAVI and discusses perspectives in Korea.

Keywords: Aortic valve stenosis; Transcatheter aortic valve replacement

INTRODUCTION

Innovations in public healthcare practices and medicines have led to a significant increase in life expectancies in developed countries. Korea has been associated with rapid increases in life expectancy as well, and its population is aging as a result. The expected age of death has increased by more than 20 years from 62 in 1970 to 83 in 2017, a change approximately twice the average of developed countries.[1)2)] Korea is on track to claim the longest average life expectancy in the world and to achieve the biggest increase in longevity over the next 2 decades.[3)] Longevity is a desirable achievement in medicine but the accompanying increases in incidence of chronic diseases, multi-comorbidity, and senility have serious implications for clinical decision-making. Given a marked decrease in rheumatic etiology, aortic stenosis (AS) is already the most prevalent valvular heart disease among degenerative diseases in developed countries and its incidence tends to increase rapidly with age.[4)] Valve replacement is the definitive treatment to extend survival after a diagnosis of symptomatic severe AS, but it is frequently accompanied by chronic coronary or pulmonary disease and the poor physical conditions that are associated with advanced age. Therefore, despite the expected benefits of improvement in symptoms, functional status, and long-term survival that come with procedures such as surgical aortic valve replacement (SAVR),[5)] candidate patients

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must be chosen carefully to ensure the procedure comes with a favorable risk-benefit ratio. Since the first pioneering procedure involving a balloon-expandable valve by Cribier et al. in 2002,[6] transcatheter aortic valve implantation (TAVI) has been available to rescue patients in high-risk conditions or with potential therapeutic contraindications, which will be more common among patients in the future. TAVI is becoming the leading treatment modality for management of advanced AS, thanks to novel devices and a series of landmark clinical trials that have expanded the indications for intermediate- to low-risk patients. More than 300,000 TAVI devices have been implanted worldwide to date, and their use is sharply increasing such that the annual volume is likely to reach at 300,000 cases by 2025. In this review, we will address the current status, problematic issues, and future directions regarding TAVI, mainly focusing on the balloon-expandable SAPIEN valve and the self-expandable CoreValve systems which are most widely used now in Korea.

CHRONICLES OF TRANSCATHETER AORTIC VALVE IMPLANTATION: COMPLEMENT OR REPLACEMENT?

Although surgical treatment has rescued many patients with symptomatic valvular diseases, a third of patients with severe AS suffered dismal consequences without undergoing valve replacement before the advent of the TAVI era.[7] Major randomized controlled trials (RCTs) and pivotal achievements of the TAVI era are illustrated in **Figure 1**. Since the Placement of AoRTic TraNscathetER Valve (PARTNER) 1 trial demonstrated promising outcomes after TAVI using the balloon-expandable Edwards valve system (Edwards Lifesciences, Irvine, CA, USA), TAVI has been considered a unique treatment for inoperable patients or an adequate alternative to SAVR in high-risk patients.[8][9] The self-expandable CoreValve revalving system (CoreValve, Irvine, CA, USA) also offers superior one-year mortality among patients with severe AS and facing an increased risk of death from surgery, as demonstrated by the CoreValve US Pivotal Trial.[10] Follow-up studies of 5-year results support using TAVI in high-risk patients.[11-13] Prospective registries in UK, France, Germany, and Italy have also approved the use of TAVI in high-risk patients.[14-19] Meanwhile, TAVI is being used not only in patients at high surgical risk but also in those with a relatively low risk profile.[20][21] Expansion of the indications for TAVI is supported by results of major RCTs that enrolled intermediate- or low-risk patients as determined by a Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) score or other coexisting conditions (**Table 1**). In the PARTNER 2 cohort A study, 2,032 patients with severe AS (mean STS-PROM score, 5.8%) randomly received either TAVI or SVAR. TAVI was not inferior to SAVR in terms of incidence of all-cause death and disabling stroke for 2 years (19.3% vs. 21.1%; hazard ratio [HR], 0.89; 95% confidence interval [CI], 0.73–1.09; p=0.001 for non-inferiority, p=0.25 for superiority).[22] Results of the randomized Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients (SURTAVI) study also described the safety and efficacy of TAVI in intermediate-risk patients.[23] Among 1,660 patients who underwent valve-replacement (mean STS-PROM score, 4.5%), the estimated incidence of all-cause death and disabling stroke was 12.6% in the TAVI group and 14.0% in the SAVR group (posterior probability of non-inferiority >0.999). Patients with a relatively lower risk were investigated in the Nordic Aortic Valve Intervention Trial (NOTION), which included 280 patients ≥70 years old with severe AS and no coronary artery disease. There was no difference in all-cause death, stroke, or myocardial infarction in at the 1-year (TAVI vs. SAVR, 13.1% vs. 16.3%; p=0.43)[24] or 5-year follow-up results (TAVI vs. SAVR, 39.2% vs. 38.5%; p=0.78).[25] A series of meta-analyses of RCTs suggested lower all-cause mortality was associated with TAVI in all patients irrespective of risk profile (HR, 0.87; 95% CI, 0.76–

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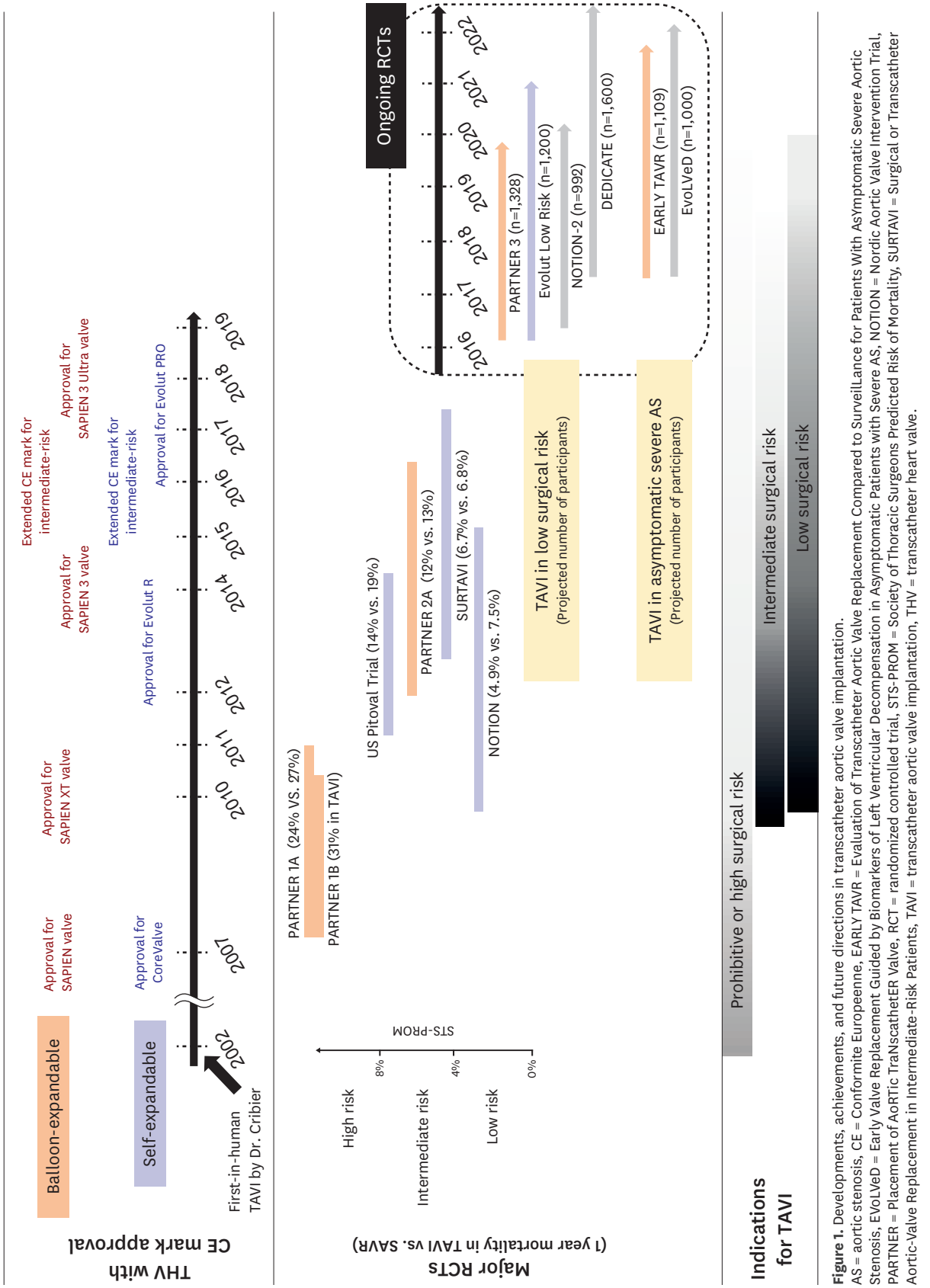

Figure 1. Developments, achievements, and future directions in transcatheter aortic valve implantation.
AS = aortic stenosis, CE = Conformite Europeenne, EARLY TAVR = Evaluation of Transcatheter Aortic Valve Replacement Compared to SurveilLance for Patients With AsYmptomatic Severe Aortic Stenosis, EvoLVeD = Early Valve Replacement Guided by Biomarkers of Left Ventricular Decompensation in Asymptomatic Patients with Severe AS, NOTION = Nordic Aortic Valve Intervention Trial, PARTNER = Placement of AoRTic TraNscatheter Valve, RCT = randomized controlled trial, STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality, SURTAVI = Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients, TAVI = transcatheter aortic valve implantation, THV = transcatheter heart valve.

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Table 1. Summary of randomized controlled trials comparing transcatheter versus surgical aortic valve replacement in patients at intermediate to low surgical risk

Characteristics	PARTNER 2 cohort A[22]	SURTAVI[23]	NOTION[24][25]
Study period	Dec 2011–Nov 2013	Jun 2012–Jun 2016	Dec 2009–Apr 2013
Participants	2,302	1,746	280
Transcatheter valves	Sapien XT	CoreValve and Evolut R	CoreValve
Study criteria	Inclusion: STS-PROM ≥4% or other intermediate-risk profile with comorbidities determined by heart team Exclusion: unicuspid, bicuspid, or non-calcified valves	Inclusion: STS-PROM 3–15% and <15% Exclusion: bicuspid or unicuspid valve	Patients ≥70 years old with severe aortic valve stenosis and no significant coronary artery disease regardless of surgical risk of death
Age and the STS-PROM score in TAVI arm	82±7 years/5.8±2.1%	80±6 years/4.4±1.5%	79±5 years/2.9±1.6%
Outcomes (TAVI vs. SAVR)			
Primary endpoint	Composite of all-cause death and disabling stroke at 2 years 19.3% vs. 21.1% (HR, 0.89; 95% CI, 0.73–1.09; p=0.001 for non-inferiority, p=0.25 for superiority)	Composite of all-cause death and disabling stroke at 2 years 12.6% vs. 14.0% (95% credible interval −5.2 to 2.3%; posterior probability of non-inferiority >0.999)	Composite of all-cause death, stroke, and myocardial infarction at 1 year 13.1% vs. 16.3%; p=0.43
All-cause death	At 1 year: 12.3% vs. 12.9%; p=0.69 At 2 years: 16.7% vs. 18.0%; p=0.45	At 1 year: 6.7% vs. 6.8%; 95% credible interval −2.7 to 2.4% At 2 years: 11.4% vs. 11.6%; 95% credible interval −3.8 to 3.3%	At 1 year: 4.9% vs. 7.5%; p=0.38 At 5 years: 27.7% vs. 27.7%; p=0.90
Any stroke	At 30 days: 5.6% vs. 6.1%; p=0.63 At 2 years: 9.6% vs. 9.0%; p=0.66	At 30 days: 3.4% vs. 5.6%; 95% credible interval −4.2 to −0.2% At 2 years: 6.2% vs. 8.4%; 95% credible interval −5.0 to 0.4%	At 30 days: 1.4% vs. 3.0%; p=0.37 At 5 years: 10.5% vs. 8.2%; p=0.67
Moderate-to-severe paravalvular leakage at 1 year	3.4% vs. 0.4%; p<0.001	5.3% vs. 0.6%; 95% credible interval 2.8 to 6.8%	15.7% vs. 0.9%; p<0.001
New permanent pacemaker implantation at 30 days	8.5% vs. 6.9%; p=0.17	25.9% vs. 6.6%; 95% credible interval 15.9 to 22.7%	34.1% vs. 1.6%; p<0.001
Life-threatening or major bleeding	At 30 days: 10.4% vs. 43.4%; p<0.001*	At 30 days: 12.2% vs. 9.3%; 95% credible interval −0.1 to 5.9%	At index hospitalization: 11.3% vs. 20.9%; p=0.03

CI = confidence interval; HR = hazard ratio; NOTION = Nordic Aortic Valve Intervention Trial; PARTNER = Placement of AoRTic TraNscathetER Valve; SAVR = surgical aortic valve replacement; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; SURTAVI = Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients; TAVI = transcatheter aortic valve implantation.
*Incidence of life-threatening or disabling bleeding was reported in the PARTNER 2A trial.

0.99; p=0.038)[26] and in those undergoing transfemoral (TF) TAVI with intermediate to low risk (HR, 0.79; 95% CI, 0.66–0.94).[27] Worldwide revenue from TAVI has been rising sharply. Reports from Germany and the US indicate the number of SAVR procedures has decreased slightly, but not as much as TAVI procedures have increased.[28] TAVI is now outstripping SAVR in terms of valve replacement for patients with severe AS. However, it is reasonable to assume that TAVI may be a complement to, rather than a replacement for, SAVR, given individualized risk factors such as frailty or senility, procedural feasibility, and patient or doctor preference and expectations.

CURRENT STATUS OF TRANSCATHETER AORTIC VALVE IMPLANTATION: ON THE WAY TO BE A UNIVERSAL TREATMENT

Expanded indication to low surgical risk

The German Aortic Valve Registry recently reported on clinical management of severe AS in 20,549 patients at low surgical risk who may be eligible for both TAVI and SAVR between 2014 and 2015.[29] Adjusted analysis demonstrated that TAVI was associated with better 30-day survival (98.3% vs. 97.0%; p=0.001) and similar 12-month survival (90.4% vs. 91.2%; p=0.368) rates compared with SAVR. With regard to the choice of treatment among low-risk patients, age was the most important factor affecting decisions involving a choice between

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TAVI and SAVR (mean age: 78.9 vs. 67.5 years, respectively). TAVI was rarely performed (<5%) in patients under 70 years old but was the predominant treatment in patients older than 75 at low surgical risk (4,760/8,439, 56%). Another study enrolling patients during two recent years suggested the possibility that TAVI could be performed in younger patients at low surgical risk. The Low Risk TAVR trial recruited 200 patients with an STS-PROM score ≤3% and a mean age of 73.6 years.[30] The study incorporated the latest strategies for TAVI, including a relatively low use of general anesthesia (25%) and maximal use of TF access (100%). TAVI led to superior outcomes with regard to the incidence of 30-day major events, including mortality, disabling stroke, and myocardial infarction, and the risk of procedure-related complications, including major bleeding (3%), new-onset atrial fibrillation (3%) and new permanent pacemaker implantation (PPI; 5%). Ongoing large, population-based randomized trials will determine whether TAVI is a valuable treatment in patients with symptomatic severe AS and low surgical risk (**Figure 1**). The PARTNER 3 trial (NCT02675114) is now enrolling patients who will undergo TAVI with Edwards SAPIEN 3 or SAVR. It is scheduled to complete enrollment and assessment of one-year all-cause mortality, all stroke, and re-hospitalization in 1,328 patients in January 2020. The Medtronic Evolut Transcatheter Aortic Valve Replacement in Low Risk Patients (NCT02701283), the NOTION-2 (NCT02825134), and the DEDICATE (NCT03112980) trials are also testing the non-inferiority of TAVI compared with SAVR among low-risk patients. Because NOTION-2 will adopt a unique criterion for enrollment of patients 75 years of age or younger, it is possible that TAVI will be an established option for the younger population if the study produces results as promising as hypothesized.

Bicuspid severe aortic stenosis

A bicuspid aortic valve is the most common congenital cardiac abnormality, occurring in approximately 1% of the general population.[31] Although clinical presentation and progress can vary, most patients with a bicuspid aortic valve may experience progressive deterioration with age and the condition is frequently associated with significant aortic valvulopathy. Atypical features of valve morphology and concomitant aortopathy may restrict the use of TAVI in early trials. However, TAVI may be associated with similar procedural success and clinical outcomes for patients with tricuspid and bicuspid aortic valves. In a study by Hayashida et al.[32] of 229 consecutive patients considered for TAVI, 21 (9%) had a bicuspid aortic valve, yet there were no differences in device success, complications, hemodynamic improvement or 30-day mortality. A propensity-score-matching study of 561 pairs of patients with bicuspid and tricuspid AS who underwent TAVI revealed comparable 2-year mortality following procedure.[33] However, patients with bicuspid AS had a significantly lower device success rate (85% vs. 91%, p=0.002), a difference that may be associated with the use of early-generation devices. Among patients implanted with new-generation devices, procedural results were improved in all patients, with no significant difference between study arms. New-generation devices provide effective sealing and resistance to migration, which may reduce procedural failure rates. In addition, experience with the proper selection of candidates, treatment planning, and procedural techniques should contribute to improved outcomes in patients with bicuspid AS. Significant differences in the incidence or morphology of bicuspid aortic valves across different ethnicities should be also considered. In a recent study of inter-ethnic differences in patients with a bicuspid aortic valve, Asians were associated with more frequent type 1 morphology and larger aortic dimensions compared with Europeans.[34] A better understanding of the association between valvular morphology (with aortic anatomy) and procedural factors (device type, size, and the use of intraprocedural imaging) may help optimize procedural successes and improve long-term prognosis. The Medtronic Low Risk Bicuspid study (NCT03635424) is an ongoing single-arm

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observational investigation that will assess patients with bicuspid severe AS at low surgical risk. An ongoing RCT (NCT03163329) will compare the efficacy of TAVI and SAVR in patients with bicuspid severe AS and intermediate surgical risk.

Overcoming complications

Despite successful outcomes in landmark RCTs that have opened a new era of TAVI, substantial concerns with complications after the procedure persist. In the PARTNER 1 cohort B trial, for example, TAVI improved the one-year survival rate (31% vs 50%, p<0.001) at the expense of 30-day incidence of stroke (6.7%) and major bleeding (16%), approximately four-fold risks compared with a conservative treatment group.[9] Similar concerns have been raised about more frequent neurologic events, including stroke or transient ischemic attack (TAVI vs. SAVR, 5.5% vs. 2.4%; p=0.04 for 30 days and 8.3% vs. 4.3%; p=0.04 for 1-year) and vascular complications (11% vs. 3%; p<0.001) in the PARTNER 1 cohort A trial.[8] Similar incidence rates for neurological events within 30 days or 12 months was reported in patients undergoing TAVI compared with those undergoing SAVR in subsequent RCTs.[10][22][24] In the SURTAVI trial, TAVI was associated with a lower incidence of 30-day (3.3% vs. 5.4%; p=0.031) and earlier recovery of quality of life after incidence of early stroke compared with SAVR.[35] Meta-analysis of RCTs including patients at low and intermediate risk showed that TF TAVI tends to decrease the risk of stroke, while transapical TAVI leads to a higher incidence of stroke.[27] Because perioperative stroke is known to be associated with a more than six-fold greater risk of 30-day mortality, preventive strategies are still essential.[36] Furthermore, subclinical cerebral infarction could be an important problem as it is only detected by diffusion-weighted magnetic resonance imaging and results in mild cognitive impairment.[37][38] Considering the highest risk of stroke occurs during the peri-procedural period accompanied with embolic debris, transcatheter cerebral protection devices have been suggested for stroke prevention.[39][40] A patient-level propensity-matched analysis recently suggested that a dual-filter cerebral protection device (Claret Medical Inc., Santa Rosa, CA, USA) led to a significant reduction in clinical events, including peri-procedural stroke (odds ratio [OR], 0.35; 95% CI, 0.17–0.72; p=0.003), and all-cause mortality plus all stroke (OR, 0.34; 95% CI, 0.17–0.68; p=0.001).[41] Further RCTs may be needed to determine the devices' efficacy on clinical events and the role of other devices. Evolution of the transcatheter valves facilitates a low delivery profile of the devices, which may contribute to the reduction in the incidence of vascular complications. However, the hostile anatomy of the iliofemoral artery may lead to poor clinical outcomes, including the incidence of vascular complications as well as immediate and late mortality.[42] In many institutes performing TAVI, careful anatomical assessment of possible vascular accesses is performed using computed tomography angiography. TF access should be considered the primary route for valve delivery, but alternative vascular accesses via transapical, transsubclavian, transaortic, and transcarotid accesses are needed if TF access is not feasible.[43] Strategic decisions concerning vascular accesses, device type, revascularization of iliofemoral arteries before TAVI, and vascular closure are needed to minimize vascular complications.

Concerns about PPI, such as a reduction in mortality with the use of the CoreValve system, have been raised despite favorable results. While the 30-day incidence of new PPI was about 7% after SAVR, it was more common in patients undergoing TAVI at intermediate (26%)[23] and high (20%)[10] surgical risk in the landmark RCTs. A systematic review illustrated that the PPI rate with the new Evolut R device was still high (14.7–26.7%) but slightly lower than that of the early-generation CoreValve device (16.3–37.7%).[44] Pre-existing conduction abnormalities such as right-bundle branch block, implantation depth, and use of balloon

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dilation were revealed to be risk factors for new PPI after CoreValve implantation.[45][46] Although it had little impact on mortality risk, new PPI seems to have unfavorable effects on left-ventricular function.[23][47][48] Long-term influences of new PPI and its preventive strategies should be further investigated in post-TAVI patients.

Moderate to severe paravalvular leakage (PVL) is considered a suboptimal result after TAVI because it is significantly associated with late mortality.[23][49] The incidence of moderate or severe PVL after TAVI, as reported in early meta-analyses of recent RCTs[50][51] has fallen slightly from 4.5–11.7% to 3.7–5.3%, including in intermediate-risk patients.[22][23] PLV is likely more common after TAVI than after SAVR considering the <1% incidence of PLV associated with it. PVL may be induced by incomplete sealing of the annulus with suboptimal positioning, calcification of the device landing zone including annulus, native leaflets, left ventricular outflow track, and prosthesis-patient mismatch.[52] Balloon post-dilation is most frequently used to diminish PLV after TAVI. Among 3,532 patients undergoing TAVI in the US CoreValve trial, balloon post-dilation was used in 782 patients (22%), most of whom were diagnosed with PVL (mild 37%, moderate or severe 58%). The study reported that the incidence of moderate to severe PVL was much lower after balloon post-dilation without an increase in neurologic events.[53] Percutaneous closure using a vascular plug was also suggested due to a high procedural success rate. Because improvement in percutaneous closure of PVL has led to comparable prognoses for surgical closure, the procedure may be more common for treatment of PLV, especially in complicated cases or in patients at excessive risk for redo SAVR.[54]

FUTURE DIRECTION OF TRANSCATHETER AORTIC VALVE IMPLANTATION: TO UNIQUE INDICATION AND BENEFIT BEYOND SURGICAL AORTIC VALVE REPLACEMENT

Asymptomatic severe aortic stenosis

Relevant symptoms and their severity are major factors in decisions regarding treatment strategies for severe AS. Current European and US guidelines recommend valve replacement for symptomatic patients in whom SAVR or TAVI is chosen by surgery-related risk and consensus discussion.[55][56] Currently, TAVI is not recommended for asymptomatic patients who may be considered for SAVR only if myocardial dysfunction or hemodynamic deterioration exist.[56][57] Valve replacement is commonly delayed until symptom onset, given the relatively slow progression of AS and perioperative risk. However, prediction of symptom onset or cardiac events is not easy in elderly patients.[58] After symptom onset in patients with severe AS, clinical deterioration accelerates, with significant (12%) risk of sudden cardiac death within 6 months, which is much higher than the risk in asymptomatic subjects (approximately 1% per year).[59][60] Timely performance of valve replacement can help avoid dismal prognoses of advanced symptomatic AS by left-ventricular dysfunction and deteriorated physical status. Perioperative risks of adverse events, the need for antithrombotic therapy, and concerns about valve durability may delay the timing of valve replacement until symptom onset accompanied with rapid decompensation. Because TAVI-related risks of mortality and other complications have declined significantly while the mortality rate after SAVR has stabilized around the onset of the TAVI era,[61][62] it seems likely that the potential benefits of TAVI will be available at advanced timings, if periprocedural risks continue to shrink. SAVR may be not appropriate for asymptomatic patients unless otherwise indicated because the expected annual mortality rate is about 1%, which may not

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justify the risk of open-heart surgery and may not even be higher than the predicted risk of mortality of SAVR in most cases. It is important to stratify high-risk subjects to receive the benefits of early valve replacement and to predict the exact risk presented by TAVI to make the treatment widely available. The Early Valve Replacement Guided by Biomarkers of Left Ventricular Decompensation in Asymptomatic Patients with Severe AS (EVoLVeD study, NCT03094143) will investigate the clinical utility of biomarkers to define proper candidates for valve replacement and the effects of early intervention (with both TAVI or SVAR) on three-year mortality and AS-related hospitalization in patients with asymptomatic severe AS. For early identification of left-ventricular decompensation, multiple markers, including cardiac troponin, electrocardiography, and the specific pattern of diffuse myocardial fibrosis on cardiac magnetic resonance, will be used in screening and randomization for early intervention or routine care in 1,000 participants. In another ongoing trial, the Evaluation of Transcatheter Aortic Valve Replacement Compared to SurveilLance for Patients With AsYmptomatic Severe Aortic Stenosis (EARLY TAVR, NCT03042104) study, 1,109 patients with asymptomatic severe AS in whom it is feasible to take a TF approach will be randomized to receive either TAVI with SAPIEN 3 valve or conservative care (**Figure 1**).

Valve-in-valve implantation and durability

Use of bioprosthetic valves has been increasing in recent decades due to senility, frailty, and high risk or contraindication of long-term anticoagulant use.[28)63)] It is likely that structural valve degeneration of bioprosthetic surgical or transcatheter valves will be more common in recipients who have longer life spans than those of bioprosthetic valves. Before the introduction of TAVI, redo SAVR was the only option for treatment of a failing bioprosthesis, leading to severe aortic regurgitation, stenosis, or both. However, redo surgery is often not feasible for elderly patients with comorbidities, and it is also associated with a higher risk of morbidity and mortality. Valve-in-valve TAVI may be an acceptable alternative, one that is less invasive, especially for high-risk patients. Meta-analysis of five observational studies of 342 patients showed that valve-in-valve TAVI was associated with a comparable incidence of procedural or 30-day mortality but with a higher risk of cumulative mortality at mean follow-up period of 18 months than is the case with redo SAVR.[64)] Valve-in-valve TAVI may have fewer favorable echocardiographic outcomes, including a higher incidence of PVL, patient-prosthesis mismatch, and greater mean pressure gradient of aortic valve after the procedure. However, a recent long-term follow-up study reported that hemodynamic stability of valve-in-valve TAVI was sustained for five years. The incidence of clinically relevant structural valve degeneration was 3.0%, which is similar to the results obtained in TAVI for native valves.[65)] Although redo SAVR has been considered the gold standard for management of a failing bioprosthetic aortic valve, valve-in-valve TAVI may gradually replace the surgery if durability and hemodynamic improvement is guaranteed. Considering the lack of sufficient long-term data beyond five years after placement, the durability of transcatheter valves should be considered when valve replacement is needed in patients with native valve disease as well as in those with a failing bioprosthesis.

Risk stratification

Currently, risk stratification for decision-making with respect to SAVR vs. TAVI depends on comprehensive discussions among clinicians and suggested risk scores. The STS-PROM score, which was developed for open-heart surgery and not transcatheter intervention, is well-correlated and accepted as a risk prediction of TAVI as well as SAVR.[66)] However, STS-PROM scores have not equally weighed mortality rates for SAVR and TAVI in recent years. Cumulative experiences and device advances have to led to a decline in the incidence

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of procedure-related mortality and complications and the pattern is likely to continue.[21)62)] Given a lower ratio of observed to expected 30-day mortality rates of TAVI compared with that of SAVR in some prospective registries, there may be a significant potential for achieving better early outcomes than risk prediction by current scoring systems.[67)68)] Subsequent study of the PARTNER 1 cohort B trial determined that low body mass index, decrease in mean gradient, elevated serum creatinine, prior vascular procedures, and occurrence of major vascular complications were unique predictors for mortality in the TAVI group.[69)] New scoring systems to predict short-term mortality in patients undergoing TAVI have been developed.[70-74)] However, as they were not sufficiently validated in other registries or large populations or did not suggest good C-statistics (>0.7) in both development and validation cohorts, they may be not ready for practical use and just have a similar value to STS-PROM score for risk prediction. Current risk scores are limited to capturing TAVI-related factors such as bleeding tendencies, aortic angulation, and size, valvular, and vascular anatomy. Although careful assessments, including preprocedural imaging, are standard procedures in most institutions operating "heart teams", such interpretations and treatment decisions are still dependent on doctors' experiences or perspectives, and the operating standards of each institution. Alternative strategies have been developed to reduce surgical burden and anesthesia according to each patient's physical status and risk. A "minimalist" approach, with or without conscious sedation, implies minimal invasiveness and brief procedures, which are particularly suitable for patients at high surgical risk or with favorable anatomy. The frailty index has been shown to significantly improve discrimination of prediction for 1-year mortality beyond that of previous risk models.[75)] Until incidences of TAVI-associated indications, complications, and outcomes are stabilized with advanced device systems, universal risk prediction specified for TAVI candidates will not be practical. Selection of candidates, devices, and procedures should be individually guided by comprehensive discussions based on a patient's medical conditions and interest, doctors' perspectives, and the capability of the institute (**Figure 2**).

Perspectives in Korea

Along with the recent explosive increase in worldwide use, TAVI is becoming more commonly used for the treatment of symptomatic severe AS in Asian countries. However, the volume of TAVI in Asian countries is less than 10% of that in western countries. There are significant obstacles against expansion of TAVI, including excessive prices, insufficient healthcare insurance coverage, and limited experiences in major cardiac centers in Korea. A recent report identified a substantial learning curve for TAVI procedures: a highly experienced operator performing >300 cases at an institute with >50 annual cases would be required to secure optimal outcomes.[76)] Because most operators and institutes may find it difficult to meet such criteria, considerable planning, preparation, and technical improvement will be required to reduce the learning curve in clinical practice before a significant expansion of TAVI in Korea can be expected. The K-TAVI registry, the first cohort study to include the 17 centers in which TAVI has been available in Korea, illustrates the current status of TAVI practice.[77)] During 24 months between June 2015 and June 2017, 576 consecutive patients with a close-to-intermediate risk profile underwent TAVI in participating centers. Their median STS-PROM score was 5.2% (interquartile range, 3.0–9.0%) and their median age was 79 years (interquartile range, 75–83 years). In patients mostly undergoing TF TAVI (98%), the incidence of one-year all-cause mortality and disabling stroke was 10.8%, which was similar in bicuspid and tricuspid severe AS. The study reported 6.0% (24/399) of the patients had moderate to severe PVL at 30-day echocardiography and 3.3% (19/576) experience major bleeding within one month after TAVI. Given that the second-year incidence of moderate

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Current indications and applications of TAVI and SAVR

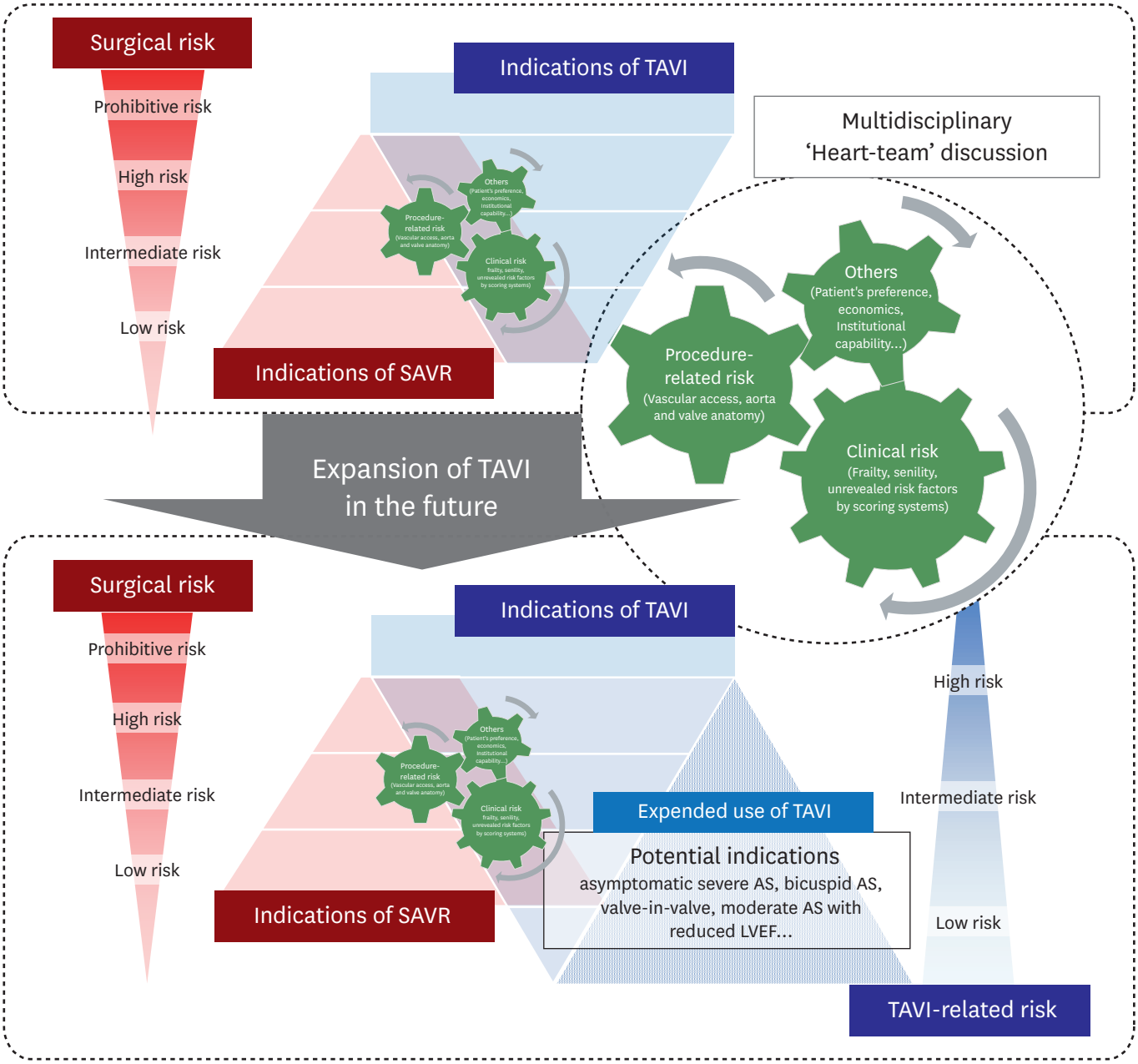

Figure 2. Current status and future expansion of TAVI compared with SAVR. The use of TAVI has rapidly increased for the treatment of severe AS with intermediate or low surgical risk in recent years. While TAVI has been indicated in symptomatic patients who require immediate replacement of a native aortic valve, expanded indications including asymptomatic severe AS, bicuspid AS, valve-in-valve, and moderate AS with left-ventricular dysfunction are under investigation. Dedicated risk stratification for TAVI would provide more accurate prediction of the potential benefits of TAVI, in addition to multidisciplinary discussion by heart team, which has and will have played a key role in decisions regarding the choice of valve replacement.
AS = aortic stenosis; LVEF = left ventricular ejection fraction; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.

or severe PVL (8.6% vs 3.7%; p=0.040) and major bleeding (5.7% vs. 1.5%; p=0.006) were significantly decreased, the favorable changes may have been influenced by the use of low-profile devices and cumulative experiences of operators in Korea. Patient refusal of surgery was the most frequent reason (68%) for TAVI among the patients with low STS-PROM score and <75 years of age in the cohort. TAVI may play a more important role in the treatment of

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severe AS given conservative tendencies among Korean patients to avoid invasive treatment. Clinical effectiveness of TAVI for such indications driven by patient refusal or unrevealed factors need to be validated by further investigations.

CONCLUSIONS

TAVI is becoming one of the major transcatheter procedures performed in the interventional cardiology field. It has played a complementary role in improving clinical outcomes of patients with severe AS but not meeting the criteria to receive SAVR. Even with technological advances and clinical evidences supporting clinical efficacy and safety, TAVI may not replace SAVR completely as long as issues of complications, long-term adverse outcomes, and durability remain. However, if current trends continue, TAVI is likely to expand its indications toward low surgical risk and even uncharted indications that have not been applicable for SAVR (**Figure 2**). Regional and ethnic differences should be also investigated to achieve optimal clinical benefits with appropriate standards of practice in Korea in the future.

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