REVIEW ARTICLE

# Updates on transcatheter aortic valve replacement: Techniques, complications, outcome, and prognosis

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**Transcatheter aortic valve replacement (TAVR) initially emerged as a therapeutic option for high-risk patients with severe aortic stenosis. Advancement in technologies since the first era of TAVRs, experience from previous obstacles, and lessons learned from complications have allowed the evolution of this procedure to the current state. This review focuses on the updates on the most current devices, complications, and outcomes of TAVR.**



*Keywords:* Aortic stenosis, Transcatheter aortic valve implantation, Transcatheter aortic valve replacement

**Contents**



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## 1. Introduction

Transcatheter aortic valve replacement (TAVR) is the procedure of introducing a nonnative aortic valve into the aortic valve position via catheters thereby without removing the native valve [1]. TAVR was initially developed to treat patients who suffered from severe aortic stenosis (AS) but were not candidates for surgical intervention [2]. Calcified AS is the most prevalent acquired valvular disorder in developed countries affecting up to 4% of elderly adults [3,4]. Surgical aortic valve replacement (SAVR) was considered the standard of care for symptomatic patients with severe AS as it had been shown to improve survival in those who were good surgical candidates without multiple comorbidities [5–7]. Nevertheless, TAVR now holds a class I recommendation in the current American College of Cardiology/American Heart Association (ACC/AHA) guidelines for management of AS in patients who have a prohibitive risk for SAVR. The first human balloon-expandable TAVR was performed by Cribier et al. [6]. It was not long afterward that Grube et al. [7] performed the first self-expanding TAVR in 2004. TAVR technologies have since then continued to evolve and improve. In this article, we will review the updates on the most current indications, devices, complications, and outcomes of TAVR.

**Abbreviations**

| | |
|---|---|
| ACC/AHA | American College of Cardiology/American Heart Association |
| AS | aortic stenosis |
| BAV | balloon aortic valvuloplasty |
| ES | Edwards Sapien |
| ESC | European Society of Cardiology |
| FDA | Food and Drug Administration |
| PPI | permanent pacemaker implantation |
| PVL | paravalvular leak |
| SAVR | surgical aortic valve replacement |
| STS | Society of Thoracic Surgeons |
| TAVR | transcatheter aortic valve replacement |

## 2. Methods

PubMed was searched for articles on AS and TAVR. Search was limited to English-language publications, and used the following search strategy: (Transcatheter aortic valve replacement) OR (TAVR) OR (Transcatheter aortic valve implantation) OR (TAVI) AND ((indications) OR (techniques) OR (complications) OR (strategies) OR (Aortic Stenosis). The references of retrieved articles were inspected for related relevant articles. These were selected and reviewed.

### 2.1. Patient selection

ACC/AHA recommendations for the choice of AVR or TAVR among patients who met indications for surgery depend mainly on the patient's surgical risk quantified by the Society of Thoracic Surgeons (STS) score, and the predicted mortality is ≥10%. Surgery risk is considered low if the STS score is <3%, intermediate if 3–8%, high risk if >8%, and prohibitive if the 30-day surgical morbidity and mortality is ≥50% because of comorbidity or serious irreversible condition [2]. An alternative tool that can be used to quantify the predicted risk of operative mortality is the Euroscore, which has similar predications when compared with the STS tool [8]. The presence of a multidisciplinary heart team is also a requirement for patient selection. The aim of the heart team, which is primarily composed of interventional cardiologists, cardiac surgeons, cardiac imaging specialists, and cardiac anesthesia specialists, is to direct the best management approach. Currently, the heart valve team is identified to play a central role in the management of severe aortic valve stenosis and is a class I recommendation as per AHA guidelines [2]. Vandvik et al. [9] evaluated TAVR versus SAVR for patients with severe symptomatic AS at low to intermediate perioperative risk. TAVR was strongly suggested over SAVR for patients aged 85 years and older even if the patient is eligible for AVR. By contrast, SAVR was strongly recommended over TAVR for patients aged 65 years and younger [9]. The role of TAVR in lower-risk patients is currently being investigated with ongoing trials including PARTNER (Placement of Aortic Transcatheter Valves) 3, which is assessing the safety and effectiveness of using the Edwards SAPIEN 3 valve (one of the newer generation valves) in patients who are at low risk for operative SAVR. This trial is expected to be completed by 2027 [10]. Moreover, another trial, ''Medtronic Transcatheter Aortic Valve Replacement in Low Risk Patients,'' is currently underway and is estimated to finish by 2026. This trial is assessing the safety and effectiveness of the Medtronic TAVR system and if it is noninferior to SAVR in the treatment of severe AS in patients with low predicted risk of operative mortality for SAVR [11].

Absolute and relative contraindications for TAVR includes the following: estimated life expectancy of less than a year, unlikely improvement of

J Saudi Heart Assoc
2018;30:340–348



*Table 1. Indications and contraindications of TAVR.*

| Indications | Contraindications |
|---|---|
| Severe AS with high or intermediate risk for SAVR | Estimated life expectancy <12 mo<br>Quality of life improvement unlikely<br>Other severe valvular disease<br>Inadequate annulus size<br>Endocarditis<br>Recent development of thrombus |

AS = aortic stenosis; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

quality of life because of other comorbidities, severe primary associated disease of other valves, and anatomical contraindications that include annulus size <18 or >29 mm, thrombus in the left ventricle, active endocarditis, and elevated risk of coronary ostium obstruction [12] (Table 1).

### 2.2. Techniques and how they evolved

In the past decade, obstacles and complications have guided the evolution of TAVR technology. In 2011, there were only two commercially available TAVR devices. These were the balloon-expandable Edwards SAPIEN (ES) (Edwards Lifesciences, Irvine, CA, USA) valve and the self-expanding nitinol CoreValve (CV) (Medtronic, Minneapolis, MN, USA) prosthesis. At that time, the only valve approved (November 22, 2011) by the US food and Drug Administration (FDA) for TAVR was the ES valve. This was a bioprosthetic tri-leaflet bovine pericardial valve mounted on a cobalt chromium frame, available in 23, 26, and 29 mm. The other major commercial aortic valve was Medtronic CV system, a tri-leaflet porcine pericardial valve mounted on a self-expanding nitinol frame. The EvolutR valve is the newest commercially available product for CV. This self-expanding valve comes in four sizes: 23, 26, 29, and 34 mm. The delivery system for the EvolutR valve can be as low as 14F, and because it is repositionable this also adds to the precision of deployment. More recently, the FDA has approved the EvolutR for intermediate-risk patients with severe AS. This approval came after the SURTAVI trial demonstrated that the EvolutR had similar outcomes compared with SAVR at 24 months [13]. The Evolut PRO is the newest platform from Medtronic. It was introduced to address the higher incidence of paravalvular leak (PVL). This system requires a 16F minimum delivery system and comes in three sizes: 23, 26, and 29 mm.

As of 2017, the FDA has also approved the expanded indication of SAPIEN 3 transcatheter heart valve for patients with AS who are at intermediate risk for death or complications associated with surgery. The ES 3 transcatheter heart valve is a biological tissue valve that is available in four diameter sizes: 20, 23, 26 and 29 mm. This valve can be delivered with a delivery sheath size of 14F. These updates and approval reflect how this procedure and its indications are evolving.

Examples of other new valves include the Lotus valve (Boston Scientific, Marlborough, MA, USA), which is a repositionable valve that allows the cardiologist to assess if the valve is in the correct position prior to full deployment, ensuring excellent placement. The REPRISE III is an ongoing trial assessing this device in high- and extreme-risk patients against other available TAVR valves. The Direct Flow Medical valve (Direct Flow Medical, Inc., Lake Forest, CA, USA) is made with hollow Dacron tubes with bovine pericardial valves. This valve is also repositionable, to allow for optimal deployment.

Another valve developed by St. Jude Medical is the Portico valve. This repositionable self-expanding valve comes in four sizes (23, 25, 27, and 29 mm) and has been also shown to be noninferior to SAVR for high- and extreme-risk patients [14].

Overall, the most recent valve generations addressed multiple technical problems that were evident in the first generations of TAVR valves including availability in smaller sizes to allow delivery through a transfemoral approach in patients with a small femoral artery caliber (14F in the SAPIEN 3 and EvolutR). The small delivery size leads to less vascular complications. Updates in technology ensure a more precise deployment leading to less PVL [15,16]. Newer generation valves, such as the SAPIEN 3, Lotus, and EvolutR, are also becoming viable options for patients with bicuspid aortic valves, as studies of first-generation valves showed unacceptable levels of PVL [15,17]. Updates in valve technology have also led to a decrease in complications and improvement in valve parameters, specifically PVL. Multiple studies have recently shown that these newer valves have significantly lower PVLs compared

with older generation valves [15,17–19]. According to the PARTNER 2 trial, PVL was found in 66% of patients, with 10.5% of patients having moderate–severe PVL at 1 year follow-up [20,21]. Comparison with the results of the Lotus valve after 1 year follow-up shows that only 13.7% of participants had PVL, none of whom had moderate to severe PVL [22].

### 2.3. Procedure description

TAVR is performed in a hybrid catheterization laboratory under cineangiography and many times with simultaneous transesophageal echocardiography (TEE). In the transfemoral approach, access to the artery is gained using an ultrasound-guided percutaneous approach followed by progressive dilation of the iliofemoral vessels until a large delivery sheath is inserted. At this point, the bioprosthetic heart valve is advanced across the native aortic valve. Balloon aortic valvuloplasty (BAV) may be performed prior to delivery especially in patients with severe calcified aortic valves. Of note, BAV should be performed after the delivery sheath is inserted to secure immediate delivery of the percutaneous aortic valve if needed in cases of severe aortic insufficiency. After correctly positioning the valve in the aortic annulus, the valve is deployed. With newer valve technology, the valve could be repositioned in case PVL is identified.

Accessing through the femoral artery is the most frequently used and the least invasive approach as the transapical and transaortic approach still require surgical exposure and orotracheal intubation with general anesthesia [23]. In the PARTNER 2 trial, 76.3% of the cohort underwent TAVR through a transfemoral approach, with analysis showing better outcomes compared with the transapical approach [24]. However, heavy arterial calcification may affect the feasibility of the transfemoral approach and might increase local and systemic complications [25]. In these cases, other approaches mentioned above could be performed instead. One study that compared the transaortic approach with the transapical approach for TAVR found significant difference in all-cause mortality that persisted for a median follow-up period of 23 months (12% vs. 40% all-cause mortality, respectively) [26]. Transfemoral and transapical accesses have similar 30-day risk of stroke in patients who underwent TAVR, but transfemoral access was associated with decreased all-cause mortality at 3 months compared with transapical and AVR although they all have similar rates of all-cause mortality at 2 years [27]. Another alternative approach is the transcaval access, which is feasible for patients with ineligible femoral access and prohibitive risk of complications from transthoracic access. In this method, the guidewire is passed into the aorta by creating a transcaval port to the aorta. These ports are closed with nitinol cardiac occluders. One study involving 100 patients showed a 30-day survival of 92% [28]. The transcarotid approach is an option for high-risk patients who are not suitable for transfemoral, transapical, subclaviam, or direct aortic approach and in those who are considered unstable for general anesthesia. An approach through local anesthesia in the right common carotid artery area can be attempted, but this requires careful monitoring of cerebral oxygen throughout the procedure [29]. Finally, the transaxillary approach for TAVR is another alternative access that can be considered if the transfemoral approach is not feasible. This approach was shown to have no significant difference in procedural success and mortality compared with the transfemoral approach but requires operator experience. Furthermore, propensity-matched comparison reflected that 2-year outcomes had lower rates of acute kidney injury, minor vascular complications, and bleeding events in the transaxillary group [30].

Fig. 1 summarizes the general technique approach.

### 2.4. Postprocedure valve care

The ACC/AHA recommends the use of aspirin 75–100 mg/d in all patients with bioprosthetic aortic valve (Class IIa, Level B). Another level C recommendation is using clopidogrel 75 mg/d for the first 6 months after TAVR in addition to lifelong aspirin 75–100 mg/d [2]. By contrast, a meta-analysis published in 2015 indicated that aspirin monotherapy after TAVR was associated with similar 30-day risk of all-cause death, acute coronary syndrome, and stroke but decreased risk of major bleeding compared with dual antiplatelet therapy [31]. As for anticoagulation after TAVR, few studies have addressed this topic. The aim of using anticoagulation after TAVR is to reduce stroke incident and valve thrombosis compared with anti-platelet therapy alone. One prospective study demonstrated that anticoagulation is not associated with increased bleeding risk compared with antiplatelet therapy after TAVR [32]. Another study demonstrated that anticoagulation for patients with atrial fibrillation who underwent TAVR did not reduce incidence of stroke while increasing risk of bleeding [33]. It is clear that

J Saudi Heart Assoc
2018;30:340–348



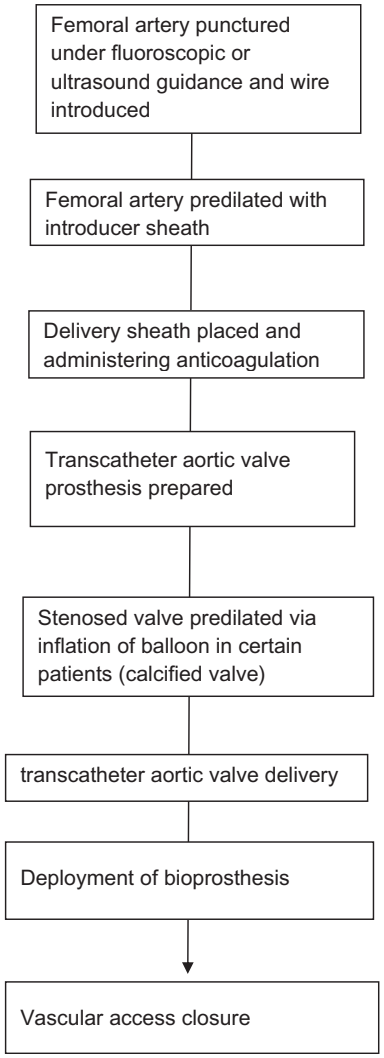


*Figure 1. General technique approach for transcatheter aortic valve replacement.*

larger evidence-based studies are necessary to elucidate the role of anticoagulation after TAVR [34]. As for infective endocarditis prevention, the AHA/ACC and the European Society of Cardiology (ESC) recommend antibiotic prophylaxis for all prosthetic cardiac valves prior to dental procedures that involve manipulation of gingival tissue or periapical region of teeth, or perforation of oral mucosa, but this is not recommended for nondental procedures (such as TEE, esophagogastroduodenoscopy, colonoscopy, or cystoscopy) in the absence of active infection [35].

### 2.5. Complications

Common complications during and after TAVR procedures include: PVL, cerebrovascular events, vascular complications, new conduction disturbance, and acute kidney injury. Mild PVL is generally considered benign, acceptable, and was reported in up to 61% of patients because of incomplete sealing. With the SAPIEN 3 valve, there was no severe PVL at 1 year. Additionally, it was shown for the first time that mild PVL did not contribute to mortality at 1 year [36].

New cerebrovascular events including ischemic lesions were detectable by magnetic resonance imaging in up to 84% of patients, of which only 4% of those were associated with clinical stroke [1]. The PARTNER 2 trial reflected no difference in rate of stroke or transient ischemic attack compared with AVR at 30 days, 1 year, and 2 years follow-up [24]. The Sentinel cerebral protection device (a filter placed in the brachiocephalic artery during the procedure to capture debris) can be used to reduce the rate of embolic stroke. The SENTINEL trial demonstrated a numerically lower rate of cerebrovascular events; however, it was not statistically significant. Local vascular complications secondary to arterial sheath insertion such as groin hematoma, vessel rupture, thrombosis, or pseudoaneurysm may occur in 5.5–20% of patients undergoing TAVR [1]. However, these vascular complications have decreased in frequency with the newer valves because of smaller delivery systems.

Onset of new atrioventricular conduction disturbances after TAVR requiring permanent pacemaker implantation (PPI) is another important complication, with 11.8% of patients in the PARTNER 2 trial requiring it 2 years after the procedure [24]. A meta-analysis that included 11,210 TAVR patients indicated a median PPI rate of 6% after ES valve and 28% after Medtronic CV implantation [37]. The PARTNER trials showed that new PPI was associated with a longer duration of hospitalization, repeat hospitalization, mortality, and repeat hospitalization at 1 year [38].

Depending on the definition used, acute kidney injury occurred in 3.4–43% of SAVR cases with up to 2.5% requiring dialysis, and in 3.4–57% of TAVR cases [39]. This was according to analysis of 12 studies including more than 90,000 patients undergoing cardiac surgery on cardiopulmonary bypass as well as 26 studies of more than 6000 patients undergoing TAVR [39].

Rare complications of TAVR of less than 1% incidence rate include myocardial perforation, valve dislodgement, need for valve repositioning, need for valve retrieval, aortic annular rupture, device embolization, and aortic dissection [1]. In a retrospective cohort study of 20,006 patients who underwent TAVR, infective endocarditis

was reported in up to 1.1% of patients with a 2-year mortality of 66.7% [40].

### 2.6. Outcome and prognosis

Overall, studies have consistently demonstrated that TAVR is associated with a decrease in mortality and improvement in quality of life for patients with symptomatic severe AS. Based on a cohort study published in 2011, TAVR and SAVR may reduce mortality compared with medical treatment in patients with symptomatic severe AS and increased surgical risk [41]. Furthermore, based on a systemic review of mostly observational studies, TAVR is associated with improvement in physical function and disease-specific measures of quality of life [42]. TAVR and SAVR may also decrease risk of mortality at 1 year compared with standard care in patients with symptomatic severe AS who are at high surgical risk [43]. Based on cohort B from PARTNER trial with baseline differences, in patients not suitable for conventional surgery, TAVR may reduce mortality, rehospitalization, and cardiac symptoms, but may increase risk of major bleeding and other vascular complications compared with standard therapy [21]. Another *post hoc* subgroup analysis of PARTNER trial published in 2013 reflected that TAVR might decrease mortality compared with standard care in nonsurgical patients with low-flow severe AS [44].

In a recently published cohort, TAVR might have up to 5.5% in-hospital mortality, 7% at 30 days, and 23.7% at 1 year [45]. This risk seems to be increased in older patients reaching up to 25% [46]. Factors that might play a role with poor prognosis include acute kidney injury, preprocedural hospitalization for heart failure, and periprocedural acute myocardial infarction [47].

In terms of procedure technique, it is suggested that transfemoral TAVR, but not transapical TAVR, may reduce 2-year mortality compared with SAVR in patients with severe AS at low or intermediate risk of perioperative death [48]. TAVR is also associated with improvement in some echocardiographic outcomes: reduced risk of prosthesis–patient mismatch compared with SAVR, but increased 2-year mortality and hospitalization in patients with a history of coronary artery bypass graft [49–51].

Comparing the outcomes of valves among each other, a recent meta-analysis suggested that balloon-expandable valves are associated with reduced risk of moderate–severe aortic regurgitation and pacemaker implantation compared with self-expandable valves in patients using TAVR [52]. Moreover, in the CHOICE trial, which was a robust, randomized-controlled trial comparing the two types of valves, suggested that balloon-expandable valves might have higher device success rates at 30 days than self-expandable valves in patients having TAVR for severe AS [53]. The success rate in the balloon-expandable group was attributed to a lower PVL rate. However, based on a prespecified secondary analysis of the CHOICE trial, balloon-expandable valves might increase risk of adverse events at 1 year compared with self-expandable valves in patients with severe AS [54]. TAVR using self-expanding bioprosthesis was reported to have 1-year event rates similar to findings in PARTNER trial cohort B in patients who have severe AS and heart failure symptoms along with prohibitive risk for SAVR [55]. More specifically, TAVR with CV self-expanding bioprosthesis is associated with lower risk of death and major cardiovascular or cerebrovascular events at 2–3 years, but increased risk of reintervention compared with SAVR [56].

In patients who underwent TAVR with SAPIEN 3 valve, lower risk of death (89.3% survival in the transfemoral approach group) and stroke (4.3% was found at 1 year compared with SAVR patients with intermediate-risk severe AS [57]. The smaller delivery system allowed 84% of the cohort to undergo a transfemoral approach, leading to a marked improvement in the rate of vascular complications and mortality [36]. These groundbreaking results led to the FDA approval of the SAPIEN 3 valve for use in patients with intermediate-risk AS.

The EvolutR valve was also assessed in intermediate-risk surgical patients. The SURTAVI trial compared the use of this valve against SAVR. The primary end point of all-cause mortality or disabling stroke was reported to be 14.0%. The complications overall were reported at a lesser frequency compared with SAVR [13]. However, a trial comparing the newest self-expandable valves and balloon-expandable valves is still underway.

### 2.7. Special population: Low flow low gradient AS, valve in valve, and bicuspid valve

TAVR has been investigated in certain special populations that pose a challenge to this evolving technique. Bicuspid aortic valves are the most congenital defect of the aortic valve. Because of the larger anatomy and elliptical shape of the aortic annulus, deploying a valve and anchoring it is more difficult. Studies have shown that there is no difference in terms of mortality and success of TAVR in bicuspid aortic valves as compared

with tricuspid aortic valves. It was noted, however, that there is an increased PVL rate among the bicuspid aortic valve groups. Newer valves, as described above, are more successful in bicuspid aortic valve TAVRs compared with older-generation valves [58].

In regard to low flow low gradient AS, the PARTNER trial demonstrated a similar outcome when comparing SAVR with TAVR at 2 years of follow-up. This group of patients has poor outcomes with medical management alone. Additionally, there is a high prevalence of concomitant Coronary Artery Disease (CAD), up to 74% in one study. Therefore, revascularization might be necessary in this cohort [59].

The feasibility of TAVR has also been evaluated in patients with degenerated bioprosthetic surgical aortic valves. Typically, these patients are high risk for redo surgical operations, and TAVR provides an attractive alternative. Analysis of the cohort in the PARTNER II trial demonstrated that TAVR improves hemodynamics and has a relatively low mortality and complications [60].

### *2.8. Future directions*

TAVR has revolutionized the management of AS in the past two decades. Rapid innovation of this technology has allowed improved outcomes, reduced complication rates, and rendered it feasible for more patients. Newer valves are being tested, including the Edwards Centera, have shown even less PVL, and other complication rates compared with the current generation of valves. As previously mentioned, the most recent studies have shown that TAVR is not inferior to SAVR for intermediate-risk patients. Two trials are in the process of evaluating the use of TAVR for low-risk patients with severe AS [61]. These advances in technology and new trials will increase the adoption of TAVR as the gold standard of treatment for severe AS.

## 3. Conclusion

TAVR is an attractive procedure to treat those patients who are at increased risk of surgical complications. Newer technologies are allowing indications for the use of TAVR to change. Combined with better patient selection and operator expertise, TAVR is trending toward being the standard of care in even patients with low surgical risk for AVR, as evidenced with the recent approval of the SAPIEN 3 valve for patients with intermediate risk for surgical AVR. Despite this evolution, however, complications exist and the operators need to be aware in order to select what technology is the best option for each patient.

## 4. Authors' contributions

All authors contributed in data gathering and literature review.

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