Review Article

Interventional Cardiology

# Benefits and limitations of transcatheter vs. surgical aortic valve replacements

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## Abstract

**Background:** Surgical Aortic Valve Replacement (SAVR) is the gold standard treatment for severe aortic stenosis. However, advanced age and interfering comorbidities combined with increased perioperative risks often make patients poor surgical candidates, necessitating the rise of the less invasive transcatheter aortic valve replacement (TAVR) approach. With the emergence of new evidence, we reviewed the literature comparing the benefits and harms of TAVR and SAVR in patients of varying surgical risk.

**Methods:** A literature search of English-language articles published from January 2009 through June 2020 was designed in Ovid MEDLINE, PubMed, up-to-date, and Scopus. We used the following search headings in different combinations: aortic stenosis; aortic valve replacement; transcatheter aortic valve replacement; TAVR; SAVR; surgical valve replacement; high risk; intermediate risk; and low risk.

**Results:** In meta-analysis, TAVR is better or non-inferior to SAVR in inoperable, high-risk, and intermediate patients when comparing mortality, rehospitalisation, severe disablement, and symptom control. These results remained consistent during follow-up at 1 year and 5 years. Evidence comparing TAVR and SAVR in low risk patients is limited, however emerging seminal trials show TAVR to have lower rates of deaths from any cause and rehospitalisation after 1 year (8.5% vs. 15.1%). In all cohorts, TAVR has significantly lower risk of major bleeding but increase risk of major vascular events, paravalvular leaks, and pacemaker implantation compared to SAVR.

**Conclusion:** TAVR has successfully provided a minimally invasive alternative for patients with significant operative and perioperative risks associated with surgical replacement. While it is a superior treatment option than SAVR in high and intermediate risk patients, the final choice remains an individual one. Further research is required in low risk cohorts, though emerging evidence indicate a likely favourable outcome for TAVR.

**Keywords:** Aortic stenosis ■ Transcatheter Aortic Valve Replacement (TAVR) ■ Surgical Aortic Valve Replacement (SAVR) ■ Cardiothoracic surgery

## Highlights

- Transaortic valve repair has lower perioperative risks than open heart surgery
- It is more efficacious in inoperable, high and intermediate surgical risk patients
- It remains unclear if benefits outweigh the risks in low surgical risk patients
- Risks include major vascular events, conduction disturbances, and valvular regurgitation
- Further research needed to find optimal anticoagulation regime post-procedurally

## Background

Aortic stenosis (AS) is the most common valvular lesion requiring intervention in the Western world. It affects approximately 5% of adults above the age of 65 years [1]. With greater life expectancy producing an ageing population, its burden is likely to increase. Developed countries have seen an epidemiological shift from rheumatic to senile valve calcification as the leading cause of AS. Its clinical course is well-defined to have a long latency period followed by an abrupt development of symptoms, often with a classic triad of exertional dyspnoea, chest pain and syncope. If left untreated, progression to cardiac failure and sudden cardiac death are seen in 60% of patients within 3 years [2].

With no medical therapy available to slow valvular deterioration, aortic valve replacement (AVR) is the only treatment shown to improve survival. Open-heart surgical AVR (SAVR) has been the mainstay treatment for severe AS, however many patients within the geriatric population are excluded as surgical candidates due to high peri-operative mortality rates linked to increased co-morbidities [3]. A step towards bridging this gap occurred with the medical innovation of the transcatheter AVR (TAVR), that successfully offset the high surgical risk with its minimally invasive technique. In 1985, French cardiologist Alain Cribier developed the first catheter-based approach of balloon aortic valvuloplasty, which later was found to be limited by restenosis within 1 year of intervention [4]. Since then, the TAVR technique has been refined with research into optimal locations for transcatheter access and the types of implantable valves. Transfemoral access is now the most common approach in current practise, though direct transaortic or transapical approaches may be considered in patients with difficult femoral access due to poor blood flow from stenosis or calcification [5].

The technological basis driving the rapid uptake of the procedure lies in its minimally invasive design that offsets the likelihood of peri-operative complications in high risk patients. Transcatheter Aortic Valve Replacement (TAVR) involves the insertion of a prosthetic valve into the stenotic aortic valve via a vascular access point without the need for open heart surgery. It is performed by an interventional cardiologist with anaesthetic support with either general anaesthetic or conscious sedation [2]. A large sheath is first inserted into the femoral artery and threaded through until it passes the native aortic valve into the left ventricle. If required, a balloon aortic valvuloplasty is conducted with a balloon catheter to pre-dilate the stenotic valve. Once achieved, the TAVR device is positioned across the native valve via fluoroscopy and deployed. The sheath is removed and the femoral artery closed using a pre-closure device. Total procedure time is comparatively short, often requiring only minimal post-operative care of cardiac telemetry and a length of stay rarely longer than 72 hours [6]. Such statistics differ greatly than those for open heart surgery, which has an average length of stay of 6 days resulting in an increase in resource utilisation and risk of nosocomial infections [7].

With the introduction of TAVR, barriers that previously hindered surgical treatment of AS have been reduced. The impediments affecting surgical scores and hence candidacy for surgical treatment include: patient age, high comorbidity rates and left ventricular dysfunction [8]. Retrospective analyses show the survival rate at 3 years in patients with symptomatic aortic stenosis who undergo surgery is 87%; in those who do not have surgery, it is 21% [4]. While it is clear that surgery in eligible patients play an important role in curative treatment, the question remains whether the risk-benefit ratio of TAVR is significant enough to annex current standard practise of SAVR.

## Methods

A literature search of English-language articles published from January 2009 through June 2020 was designed in Ovid MEDLINE, PubMed, up-to-date, and Scopus. The comprehensive review used the following search headings in different combinations: aortic stenosis; aortic valve replacement; transcatheter aortic valve replacement; TAVR; SAVR; surgical valve replacement; high risk; intermediate risk; and low risk. We dually screened abstracts and full-text articles. Case reports and articles written in languages other than English were excluded. The remaining papers were then collated and critically appraised, utilizing the most recent literature wherever appropriate. The review was conducted in June of 2020.

## Discussion

### *TAVR vs. SAVR: Benefits*

With the introduction of TAVR, multiple clinical trials have been conducted in the last decade comparing the benefit and efficacy of the new technique with previous practise. The underlying sentiment of a large volume of randomised data supports the use of TAVR in a variety of patient groups. Its benefits were first demonstrated in the highest risk patients before extending into lower risk cohorts. Patients were risk stratified according to their surgical risk based on the Society of Thoracic Surgeons (STS) score and the consensus of their heart team, with all patients having severe as the indication for surgical intervention [5]. The score takes into consideration a variety of variables affecting mortality and morbidity before giving an arbitrary score. STS score predicting mortality >8% is considered high risk, while those with predictive mortality of 4-8% are intermediate risk and those <4% are considered low risk [8].

### *High risk*

The long-term efficacy of TAVR in high risk patients is well-established. The Placement of Aortic Transcatheter Valve 1B trial (PARTNER 1B) was the first large scale trial to compare TAVR against standard medical therapy in high-risk patients deemed inoperable [9]. It consisted of 358 patients in over 21 global centers, with a primary end point of the rate of death from any cause. The trial found that TAVR had a reduction of 20% in death and 29% in rehospitalisation at one year post-intervention compared to SAVR. It was also associated with a significant reduction in symptoms based on the use of the New York Heart Association (NYHA) Classification and results from the 6-minute walk test. These results were mirrored in the PARTNER 1A trial which was designed to evaluate the outcome of TAVR versus SAVR in patients categorised as high risk but still operable [10]. 1-year all-cause mortality was 24% in TAVR compared to 26% in SAVR, meeting the non-inferior criteria. This is reaffirmed in the results of the CoreValve U.S. Pivotal High Risk Trial, which showed that all-cause mortality rates after 5 years were 55.3% for the TAVR cohort and 55.4% for the SAVR cohort, and concluding no clinical difference between the two [11]. Despite this, risk of stroke and other vascular complications were found to be higher in TAVR, and are discussed further in section 3.2.

### *Intermediate risk*

The PARTNER 2A trial was conducted next to analyse the benefits of the new procedure in the next risk group down [12]. It contained 2032 patients at intermediate surgical risk and were randomised to TAVR using a balloon-expandable valve or SAVR. It concluded that the relative risk of adverse clinical outcomes (with the endpoint of all-cause death or disabling stroke) at 2 years was similar between TAVR and SAVR, making the new procedure non-inferior in the intermediate risk group. When these cohorts were followed up again, 5 years after the intervention, there was still no significant difference in the incidence of death or disabling stroke [13]. These results were similarly emulated in the latest multinational Surgical or Transcatheter Aortic-Valve Implantation (SURTAVI) trial which alternatively used self-expanding valves [14]. Both the PARTNER 2A and SURTAVI trials uncovered additional benefits of the TAVR arm to have significantly less acute kidney injuries by 5% and new onset atrial fibrillations by 18%; a research category that was not studied in high risk patients [15].

While lower mortality rates undoubtedly attribute to the success of any medical intervention, the effect on quality of life (QOL) is an equally important consideration. This is especially significant in elderly patients, who often have multiple comorbidities and value comfort over the prolongation of survival. A substudy of the PARTNER 2A trial conducted by Baron et al. assessed the health status of intermediate-risk patients who had undergone either TAVR or SAVR at 1 month, 1 year, and 2 year time intervals based on the Kansas City Cardiomyopathy Questionnaire overall score (KCCQ-OS) as the primary QOL scale [16]. The baseline pre-operative health status was significantly impaired in both groups, with a combined mean score of 53 correlating to NYHA class III symptoms. Post-procedure scores at 1 month revealed considerable improvement in both cohorts, though substantial improvement (of greater than 20 points) was greater in transfemoral TAVR than SAVR (43.8% vs. 26.9%). As a result, TAVR elicited a notably greater early health status improvement compared to SAVR according to KCCQ-OS scores. However, at the 1 and 2 year intervals, no significant difference in health-related QOL was seen between the two cohorts (with rates of moderate or substantial improvement in TAVR and SAVR being 71.1% vs. 68.9%, and 67.2% vs. 66.2% respectively). The study concluded that patients who were treated with TAVR and SAVR demonstrated substantial and durable improvements in health status from baseline through to 2 years (with an increase of 16 to 22 KCCQ-OS points at 1 year, and a further similar increase at the 2 year follow up mark). Such results prove favourable for TAVR by providing reassurance against the higher rates of paravalvular aortic regurgitation and pacemaker requirements associated with the procedure [12,16]. In addition, when integrating mortality rates and QOL into a single endpoint, transfemoral TAVR is evidenced to be statistically more beneficial than SAVR at the 1 month, 1 year and 2 year time points, suggesting a sustained overall benefit with its implementation.

### *Low risk*

The Nordic Aortic Valve Intervention (NOTION) trial was the first published randomised trial assessing the use of TAVR in low risk patients [17]. It included 280 patients and aimed to show superiority of TAVR, but was underpowered. Instead it demonstrated similar rates of all cause death, stroke or vascular events at 2 years between the two procedures. These results lie concordant with those recently published in the multicentre, randomised PARTNER 3 trial comparing 950 surgical repair patients with 948 undertaking TAVR [18]. It found the primary endpoints of death from any cause, stroke or rehospitalisation at 1 year to be lower in TAVR (8.5% vs. 15.1%), and met the requirements for both non-inferiority and superiorirty. Secondary endpoints at 30 days also favoured TAVR with lower rates of stroke than surgery (0.6% vs. 2.4%), lower new-onset atrial fibrillation (5.0% vs. 39.5%), shorter index hospitalisation (3 days vs. 7 days), and lower risk of poor treatment outcomes (death or low

KCCQ score). Patients who underwent TAVR had more rapid improvements in the NYHA class, 6-minute walk-test distance, and KCCQ score than those who underwent surgery. However, conflicting results have arisen in recent literature with the OBSERVANT study; an observational prospective cohort study of 3402 patients conducted across 93 Italian centers [19]. While it demonstrated similar 30-day survival rates between TAVR and SAVR, the survival rate after 3 years varied considerably in favour of SAVR (72% for TAVR and 83% for SAVR). Moreover, incidence rates for cardiac tamponade, major vascular events and valvular regurgitation were more frequent in TAVR, with a clear conclusion from the study that SAVR was superior to TAVR in low surgical risk patients. Despite this, it is of note that such discrepancies in results are likely explained by selection bias and the limited exclusion criteria applied in the study (containing patients with coronary artery disease, on chronic dialytic treatment, with history of cardiac surgery and coronary revascularization, and prior stroke). Similarly, the lack of randomisation in the latter brings in the potential of selection bias, heralding a need for ongoing multinational studies to determine the long-term role of TAVR in low-risk patients [18,19].

## TAVR vs. SAVR: Limitations

### *Stroke*

Ischemic cerebrovascular events are a well-documented complication of TAVR. Common causes are related to formation of thrombi on intravascular equipment, passage of stiff instruments through calcified vessels displacing emboli, balloon valvuloplasty, and the implantation of the valve itself [20,21]. While cerebral MRI reveal incidence rates of up to 85% post-TAVR, only 3% of strokes are clinically significant, with higher prevalence's in very old patients [22]. Early seminal trials show the risk of TAVR related-stroke in high risk patients in the first 30 days to be significantly higher than SAVR (5.5% vs. 2.4%), with half of these strokes occurring within the first 24 hours [23]. A similar trend is seen at 1-year (6.0% vs. 3.2%). However, follow-up studies reveal that such a risk does not extend into lower risk cohorts. 5 year outcomes from the PARTNER 2A trial found TAVR to be noninferior to SAVR for the primary endpoint of mortality/disabling stroke in intermediate-risk patients (47.9% and 43.4%, respectively) [13]. Similar conclusions were drawn from the PARTNER 3 trial for low risk patients, which favoured TAVR over surgery at both 30 days and 1 year for stroke incidence (0.6% vs. 2.4% at 30 days, and 1.2% vs. 3.1% at 1 year) [15,24]. This likely reflects advancement of design and performance of new devices that include increased flexibility and smaller delivery systems in patients of lesser frailty [25]. To reduce the risk of stroke, aspirin, clopidogrel, or warfarin has been used in TAVR patients. Similarly, embolization-protection devices and deflectors that can redirect emboli from the arch downstream are being developed and evaluated, but no data of date support the clinical benefit of these devices [21,26,27].

### *Pacemakers*

The close proximity of the aortic arch to the atrioventricular node makes the TAVR procedure highly susceptible to conduction injuries and the need for permanent pacemaker implantation. This tissue damage is compounded by the combination of trauma, ischemia and oedema that often accompany implantation [28]. Common injuries include high degree AV block and new onset of left ventricular bundle branch block. Collated data from recent RCT's on balloon-expandable and self-expandable valves found the rates of permanent pacemaker insertion to be 12% and 18% respectively, in comparison to SAVR which reported rates of 7% at 30 days [9,15,29,30]. While such complications are often dependent on physician skill, increasing patient age and the associated frailty are confounding factors when determining the likelihood of requiring a pacemaker. As a result, monitoring the rates of pacemaker dependency in younger cohort's post-TAVR is essential to ascertain whether current data reflects the true risk associated with the procedure, or if it is an independent health outcome common in elderly patients [21].

### *Valve durability*

With the success of TAVR resulting in its adoption into younger populations, the question of the long-term durability of valves becomes pertinent. Currently, data on valve longevity is only published to 6 years post-implantation at most. The ADVANCE study followed 996 patients with self-expanding valves and found 5-year valve dysfunction rate of 2.6% [31]. Similar encouraging results are seen in the 6 year follow-up in the NOTION trial, that evaluated bioprosthetic valve durability in lower risk patients, and concluding structural valve deterioriation to be significantly greater for SAVR than TAVR (24.0% vs. 4.8%), whereas bioprosthetic valve failure that accounted for valve-related death and aortic valve intervention was low and similar for both groups (6.7% vs. 7.5%) [32]. While medium-term valve durability shows promising results, long-term data is required to confirm these findings and gauge the durable efficacy of TAVR in patients with increasingly greater life expectancies.

### *Paravalvular leak*

Higher rates of paravalvular leaks (PVL) are observed in TAVR than SAVR [33]. This is associated with incorrect sizing or placement of bioprosthetic valves, or under-expansion of it, often leading

to aortic regurgitation and increased mortality rates. The recent PARTNER 2A trial that observed contemporary valves found TAVR to have a PVL complication rate of 12% compared to 0.9% in SAVR [12]. While this conferred an increased risk of all-cause mortality in high risk patients, it found that moderate to low PVL was well tolerated by patients. Management of PVL is dictated by its cause, including paravalvular plugs or balloon post-dilation for incomplete sealing, or intra-valve procedures for misplacement. Advancement in pre-procedural planning and prosthesis design is expected to produce a marked reduction in PVL incidence and hence alleviate it as a limitation of TAVR [33,34].

The overall cost-benefit ratio leans in favour of continuing integration of the TAVR procedure into clinical practise. It is important to acknowledge that the high procedural complication rate reflects the frailty and comorbidity of the target population, along with the limitation of novel delivery technology and procedural learning curve. Mitigation of these limitations is likely to occur parallel to technological advancement and the evolution of device delivery systems with the potential future focus on the patient's individualized anatomy of their aorto-valvar complex [21].

## Appropriateness of Use

Current indications for TAVR remain limited due to lack of bulk data to allow for an evidence-based integration into clinical guidelines. Thusfar the conclusions of the aforementioned RCTs support TAVR as being advantageous in high risk groups, and agree that further research is required for low risk cohorts. The challenge remains to identify specific subgroups of patients in the intermediate risk cohort who would benefit most from TAVR. While there are international guidelines that continue to stratify recommendations by STS scores (Table 1) [5].

Concluded in their narrative review that in the absence of local guidelines and in the interim of awaiting contemporary Australian TAVR registry data, TAVR should be conducted in inoperable or high surgical risk patients [5]. They further recommended that intermediate-to-low risk patients be considered on a case-by-case basis when physicians determine that the STS score does not adequately capture perceived surgical risk.

As a result, creating strict criteria for patient suitability is central to the appropriate use of TAVR. The STS scoring system combined with physician clinical judgement has established a robust system to determine technical suitability. However, as the procedure becomes increasingly available with less technical challenges, the focus has shifted to identifying patients in whom the procedure may be futile; changing the question from whether we can to whether we should [5]. This is particularly pertinent in TAVR as AS is usually a senile condition that occurs in later years of patients lives. Integral parts in determining futility include the lack of medical efficacy judged by the physician, and a lack of meaningful survival as judged by the patient [2,4]. Hence, assessing futility requires combined input from physician, the patient, and family, ensuring that the dynamic health care goals of patients are met.

While the benefits of TAVR over SAVR are recognizably significant, steps need to be taken to lessen the associated health costs if it is to remain appropriate in medical practise. Cerebrovascular events are the top complication related to TAVR, though the optimal antiplatelet or anticoagulation regime remains unclear [35]. The RESOLVE and SAVORY registries both are single-center prospective registries compiled between 2014 and 2017 of patients who underwent TAVR or bioprosthetic SAVR to study the rates of subclinical leaflet thrombosis (SLT) and the effect of novel oral anticoagulants (NOACs) on incidence rates [36]. Compiled data found SLT to be assosciaed with increased rates of TIA's and

**Table 1:** International guidelines for TAVR indication [32,33].

| | Calculated surgical risk | | | |
|---|---|---|---|---|
| | **Inoperable** | **High** | **Intermediate** | **Low** |
| American Guidelines* | TAVR: Class I SAVR: NA | TAVR: Class I SAVR: Class I | TAVR: Class IIa SAVR: Class I | TAVR: not recommended SAVR: Class I |
| European Guidelines** | TAVR: Class I SAVR: NA | STS score>4%; decision by multidisciplinary team based on individual characteristics, with TAVR favoured in older patients suitable for transfemoral access | | TAVR: not recommended SAVR: Class I |

Note: *American College of Cardiology and American Heart Association [32]. **European Society of Cardiology and European Association for Cardio-thoracic Surgery [33]. NA: Not Applicable; SAVR: Surgical Aortic Valve Repair; STS: Society of Thoracic Surgery; TAVR: Transcatheter Aortic Valve Repair

strokes, and to occur more often after TAVR (13%) than SAVR (4%). However, such outcomes were effectively mitigated with either warfarin or a direct oral anticoagulant, but not with dual antiplatelet therapy, with incidence of thrombosis occurring at 4% and 15% respectively. Secondary outcomes found NOAC's to be equally as effective as warfarin (3% vs. 4%) at preventing SLT's. Yet concerns about the absolute efficacy of these regimes are raised in the GALILEO trial that was prematurely terminated due to safety concerns [37]. It aimed to evaluate a rivaroxaban-based strategy compared with standard dual antiplatelet therapy (DAPT) among patients who underwent TAVR, though only 42% of patients had reached the primary outcome at the time of termination. It concluded that Rivaroxaban was not effective at preventing major adverse cardiovascular events (including MI, stroke, DVT/PE, symptomatic valve thrombosis, and systemic thromboembolism) with incidence of 12.7% vs. 9.5% in the DAPT strategy. Additionally, it was associated with increase in major cardiovascular events, an increase in all-cause mortality, and an increase in majorly bleeding events (5.6% vs. 3.8%). Interestingly, the leaflet thrombosis substudy arising from the GALILEO trial revealed lower incidence of leaflet thrombosis with rivaroxaban in 4D-CT imaging, though the mechanism of this remains unknown [38]. The uncertain clinical significance of these findings, combined with the unfavourable results of the parental trial, means at present there is no evidence-based role for prophylactic oral anticoagulation after TAVR without established indication. Recently revised 2017 American Heart Associated (AHA) guidelines recommend patients should be on DAPT for the first 6 months, after which they should continue with life-long aspirin [39]. The guidelines for anticoagulation differ based on the type of valve; bioprostheses patients should be anticoagulated with VKA for at least 3 months up to 6 months based on patient bleeding risk, and mechanical valves should have lifelong VKA [39]. However, it is important to note that such recommendations are established largely on expert opinion, and further research is required to elucidate optimal blood-thinning regimes to reduce post-TAVR morbidity and mortality.

## Conclusion

The introduction of TAVR has revolutionised the outlook of AS patients. It has provided a minimally invasive alternative for patients with significant operative and perioperative risks associated with surgical replacement. In seminal trials, TAVR in inoperable or high-risk patients is found to be better or non-inferior to medical therapy and SAVR in respect to endpoints of mortality, rehospitalisation and severe disablement. While similar results are surfacing for intermediate risk, further research is required in lower risk cohorts before the expansion of TAVR can be made available to all severe AS patients. To do so, further clinical trials are needed to identify indications and contraindications for specific valves and vascular access methods, which in turn would help physicians tailor treatments to patients.

Optimising perioperative management remains a central factor in the success of TAVR outcomes. Establishing optimal antiplatelet and anticoagulation regimen is important in mitigating the biggest complication of ischemic stroke related to the procedure. Procedural complications of valvular leaks and durability need to be addressed as transcatheter technology improves with second generation devices and increased operator experience. Achieving this will result in a significant decrease in the already small mortality and morbidity rates that in turn has the potential of cementing TAVR as the gold standard in clinical practise in the near future.

## Declarations of Interest

None.

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## Disclosures

Nil.

## References

1. Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: A population-based study. Lancet. 368(9540): 1005-1011 (2006).
2. Alsara O, Alsarah A, Laird-Fick H. Advanced age and the clinical outcomes of transcatheter aortic valve implantation. J Geriatr Cardiol. 11(2): 163-70 (2014).
3. Iung B, Cachier A, Baron G, et al. Decision-making in elderly patients with severe aortic stenosis: Why are so many denied surgery? Eur Heart J. 26(24): 2714-2720 (2005).
4. Díez JG. Transcatheter aortic valve implantation (TAVR): The hype and the hope. Tex Heart Inst J. 40(3): 298-301 (2013).
5. Nelson AJ, Montarello NJ, Cosgrove CS, et al. Transcatheter aortic valve implantation: A new standard of care. MJA. 209(3): 136-141 (2018).
6. Chopra M, Luk NHV, Backer OD, et al. Simplification and optimization of transcatheter aortic valve implantation-fast-track course without compromising safety and efficacy. BMC Cardiovasc Disord. 18(1): 231 (2018).
7. Arora S, Strassle PD, Kolte D, et al. Length of stay and discharge disposition after transcatheter versus surgical aortic valve replacement. Circ Cardiovasc Interv. 11(9): e006929 (2018).
8. Grover FL, Shahian DM, Clark RE, et al. The STS national database. The Annals of Thoracic Surgery. 97(1): S48-S54 (2014).
9. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med.

363(17): 1597-607 (2010).

10. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 364(23): 2187-2198 (2011).
11. Gleason TG, Reardon MJ, Popma JJ, et al. 5-Year outcomes of self-expanding transcatheter versus surgical aortic valve replacement in high-risk patients. J Am Coll Cardiol. 72(22): 2687-2696 (2018).
12. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med. 374(17): 1609-1620 (2016).
13. Makkar RR, Thourani VH, Mack MJ, et al. Five-year outcomes of transcatheter or surgical aortic-valve replacement. J Am Coll Cardiol. 382(9): 799-809 (2020).
14. Reardon MJ, Mieghem NMV, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. N Engl J Med. 376(14): 1321-1331 (2017).
15. Reed S, Agoritsas T, Manja V, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic stenosis at low and intermediate risk: Systematic review and meta-analysis. BMJ. 354: i5130 (2016).
16. Baron SJ, Arnold SV, Wang K, et al. Health status benefits of transcatheter vs. surgical aortic valve replacement in patients with severe aortic stenosis at intermediate surgical risk: Results From the PARTNER 2 Randomized Clinical Trial. JAMA Cardiol. 2(8): 837-845 (2017).
17. Søndergaard L, Steinbrüchel DA, Ihlemann N, et al. Two-year outcomes in patients with severe aortic valve stenosis randomized to transcatheter versus surgical aortic valve replacement. Circ Cardiovasc Interv. 9(6): e003665 (2016).
18. Mack MJ, Leon MB, Thourani VH, et al. Transcathere aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 380(18): 1695-1705 (2019).
19. D'Errigo P, Barbanti M, Ranucci M, et al. Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis: Results from an intermediate risk propensity-matched population of the Italian observant study. Int J Cardiol. 167(5): 1945-52 (2013).
20. Kahlert P, Knipp SC, Schlamann M, et al. Silent and apparent cerebral ischemia after percutaneous transfemoral aortic valve implantation. Circulation. 121(7): 870-878 (2010).
21. Terré JA, George I, Smith CR. Pros and cons of Transcatheter Aortic Valve Implantation (TAVI). Ann Cardiothorac Surg. 6(5): 444-452 (2017).
22. Nombela-Franco L, Webb JG, Jaegere PP, et al. Timing, predictive factors, and prognostic value of cerebrovascular events in a large cohort of patients undergoing transcatheter aortic valve implantation. Circulation. 126(25): 3041-3053 (2012).
23. Kahlert P, Al-Rashid F, Döttger P, et al. Cerebral embolization during transcatheter aortic valve implantation. Circulation. 126(10): 1245-55 (2012).
24. Mack MJ, Leon MB, Thourani VH, et al. Transcathere aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 380(18): 1695-1705 (2019).
25. Panayiotides I, Nikolaides E. Transcatheter aortic valve implantation (TAVR): Is it time for this intervention to be applied in a lower risk population? Clin Med Insights Cardiol. 8: 93-102 (2014).
26. Bagur R, Solo K, Alghofaili S, et al. Cerebral embolic protection devices during transcatheter aortic valve implantation. Stroke. 48(5): 1306-1315 (2017).
27. Haussig S, Mangner N, Dwyer MG, et al. Effect of a cerebral protection device on brain lesions following transcatheter aortic valve implantation in patients with severe aortic stenosis: The CLEAN-TAVR randomized clinical trial. JAMA. 316(6): 592-601 (2016).
28. Moreno R, Dobarro D, Lopez de Sa E, et al. Cause of complete atrioventricular block after percutaneous aortic valve implantation. Circulation. 120(5): e29-e30 (2009).
29. Wendler O, Schymik G, Treede H, et al. SOURCE 3 registry: Design and 30-day results of the European postapproval registry of the latest generation of the SAPIEN 3 transcatheter heart valve. Circulation. 135(12): 1123-32 (2017).
30. Orajja P, Kodali S, Reardon MJ, et al. Outcomes for the commercial use of self-expanding prostheses in transcatheter aortic valve replacement: A report from the STS/ACC TVT registry. JACC Cardiovasc Interv. 10(20): 2090-2098 (2017).
31. Gerckens U, Tamburino C, Bleiziffer S, et al. Final 5-year clinical and echocardiographic results for treatment of severe aortic stenosis with a self-expanding bioprosthesis from the advance study. Eur Heart J. 38(36): 2729-38 (2017).
32. Søndergaard L, Ihlemann N, Capodanno D, et al. Durability of transcatheter and surgical bioprosthetic aortic valves in patients at lower surgical risk. J Am Coll Cardiol. 73(5): 546-553 (2019).
33. Beohar N, Kirtane AJ, Blackstone E, et al. Trends in complications and outcomes of patients undergoing transfemoral transcatheter aortic valve replacement: Experience from the partner continued access registry. JACC Cardiovasc Interv. 9(4): 355-363 (2016).
34. Athappan G, Patvardhan E, Tuzcu EM, et al. Incidence, predictors, and outcomes of aortic regurgitation after transcatheter aortic valve replacement: Meta-analysis and systematic review of literature. J Am Coll Cardiol. 61(15): 1585-1595 (2013).
35. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 38(36): 2739-2791 (2017).
36. Chakravarty T, Sondergaard L, Friedman J, et al. Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study. Lancet. 389(10087): 2383-2392 (2017).
37. Dangas GD, Tijssen JGP, Wöhrle J, et al. A controlled trial of rivaroxaban after transcatheter aortic-valve replacement. N Engl J Med. 382: 120-129 (2020).
38. De Backer O, Dangas GD, Jilaihawi H, et al. Reduced leaflet motion after transcatheter aortic-valve replacement. N Engl J Med. 382(2): 130-139 (2020).
39. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. Circulation. 135(25): e1159-e1195 (2017).