Review Article | Omics Sciences

Outcomes of transcatheter aortic valve replacement in patients with hypertrophic cardiomyopathy: a systematic review

Karsten Parker[1], Abdelrahman Aljadi[2], Uzoma N. Ibebuogu[2]^

[1]University of Tennessee Health Sciences Center, College of Medicine, Memphis, TN, USA; [2]Division of Cardiovascular Diseases, Department of Medicine, University of Tennessee Health Sciences Center, Memphis, TN, USA

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Correspondence to: Uzoma N. Ibebuogu, MD, FACC, FSCAI. Division of Cardiovascular Diseases, Department of Medicine, University of Tennessee Health Sciences Center, 956 Court Avenue, Suite A 312, Memphis, TN 38163, USA. Email: uibebuog@uthsc.edu.

Background: Transcatheter aortic valve replacement (TAVR) is a guideline recommended minimally invasive cardiovascular procedure used to replace severely stenosis aortic valves. Patients with severe aortic stenosis (AS) and co-existing hypertrophic cardiomyopathy (HCM), a common defect affecting the left ventricle of the heart, have been excluded from TAVR studies due to perceived challenges to optimal valve implantation in this group of patients because of the hypertrophied left ventricle that can result in an abrupt drop in afterload from a newly replaced and more efficient aortic valve. This exclusion has resulted in paucity of data on this patient population. This study aims to review outcomes in patient with HCM undergoing TAVR for severe AS.

Methods: Using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Statement, we performed a systematic literature search of published outcomes regarding TAVR in HCM patients to provide some insight in this patient population.

Results: Our study showed that TAVR had significantly lower rates of in-hospital mortality, bleeding requiring a blood transfusion, invasive mechanical ventilation, acute kidney injury, vascular complications, and decreased length of stay (LOS) compared to surgical aortic valve replacement (SAVR) in our study population of 836 subjects from 11 publications. Our study is not a randomized controlled trial, which limits its generalization.

Conclusions: In severe AS patients with HCM, TAVR results in better outcomes compared to surgery.

Keywords: Aortic stenosis (AS); hypertrophic cardiomyopathy (HCM); transcatheter aortic valve replacement (TAVR)

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Introduction

Transcatheter aortic valve replacement (TAVR) is a guideline recommended, minimally invasive procedure used to replace stenosed aortic valves (1). Published data show TAVR to be comparable or better to surgical aortic valve replacement (SAVR) in terms of outcomes, including similar follow-up rates of stroke and a reduced risk of major bleeding events, new-onset atrial fibrillation and shorter hospitalizations (2-5). One unexplored area of interest with regards to TAVR is in patients with hypertrophy cardiomyopathy (HCM) since prior studies have excluded HCM with or without obstruction (2,6,7). HCM is a common left ventricular heart

^ ORCID: 0000-0002-1789-8254.

defect with an estimated prevalence in the global population of 1:200 and is characterized by cardiac myocyte disarray and hypertrophy (8). HCM can lead to hemodynamic issues in the left ventricle, specifically a phenomenon known as left ventricle outflow tract obstruction (LVOTO) (9). LVOTO is potentially fatal if left untreated due to complications with increased afterload from blood flow out of the left ventricle being obstructed, leading to further left ventricular hypertrophy (10). TAVR in HCM patients is a difficult procedure because the hypertrophic left ventricular septum can adapt itself to a stenotic aortic valve. Once the aortic valve is replaced, symptoms of HCM such as syncope, heart failure, shortness of breath can be unmasked. Whereas HCM was an exclusion criterion for patients with severe aortic stenosis (AS) undergoing TAVR, several published case reports describe successful TAVR in patients with HCM. The aim of our review is to describe the published outcomes of severe AS patients with HCM undergoing TAVR. We present this article in accordance with the PRISMA reporting checklist (11) (available at https://atm.amegroups.com/article/view/10.21037/atm-24-41/rc).

Methods

A systematic literature search for outcomes regarding TAVR in HCM patients was conducted. A review of all relevant reports published in English from 2010 to 2023 including case reports, case series and original reports was performed by three reviewers (K.P., A.A., U.N.I.) working independently. The literature search used a combination of two keyword search term groups. Prospective keyword search terms used in the first group of were "Transcatheter aortic valve replacement", "Transcatheter aortic valve implantation", "TAVR" and "TAVI". The second group of keyword search terms initially only included "hypertrophic cardiomyopathy". Later, various permutations to the term such as "left ventricular outflow tract obstruction", "asymmetric septal hypertrophy" and "suicide left ventricle" were added to the second keyword group due to their frequent use in place of the phrase "hypertrophic cardiomyopathy" in the literature. The keyword groups were enclosed with parentheses to limit results to the exact keywords. The operator AND was used between the first and second keyword groups to exclude papers that did not contain both the first and second keyword groups. PubMed and EMBASE were the databases used for this literature search. PubMed and EMBASE articles suggested by citation matching were also reviewed and included in the study. An additional manual search through the citations of the included reports found through the initial search was conducted, with no additional papers being added. *Figure 1* shows the PRISMA statement. Sixteen unique keyword group combinations were used in the search, returning a total of 25 unique articles to review. A total of 53 publications were initially identified. Twenty-six publications were duplicates and were removed. Fourteen publications were removed as clinical outcomes were not reported. Citations drawn from selected reports as well as citation matching through the databases produced 9 case reports and 2 original research describing outcomes of TAVR patients with HCM. Aggregate data approach was used for our review. Proportions and mean with stand deviation was used for analysis. Primary analysis of the data was performed by measuring frequencies and descriptive statistics, including mean and standard deviation (SD).

Highlight box

Key findings

- In severe aortic stenosis (AS) patients with hypertrophic cardiomyopathy (HCM), transcatheter aortic valve replacement (TAVR) results in better outcomes compared to surgery.

What is known and what is new?

- Surgery is treatment modality for severe AS patient with HCM.
- Our manuscript showed that TAVR results in better outcomes for severe AS patients with HCM.

What is the implication, and what should change now?

- A randomized controlled study is needed to further study this group of patients.

Results

A total of 11 publications describing 836 patients with HCM that underwent TAVR were identified in the literature search. *Table 1* summarizes relevant data regarding the included reports (5,6,12-20). The mean age of the study population was 79.6±10 years and 78% of the patients were female. Among the included publications that reported on valve type, the balloon expanding Edwards SAPIEN (Edwards Lifesciences. Irvine, CA, USA) valve was used in 89% of the patients compared to the self-expanding Medtronic CoreValve (Medtronic. Minneapolis, MN, USA) that was used in 11% of patients. The identified articles infrequently reported New York Heart Association (NYHA) class, frailty score, interventricular septum thickness or

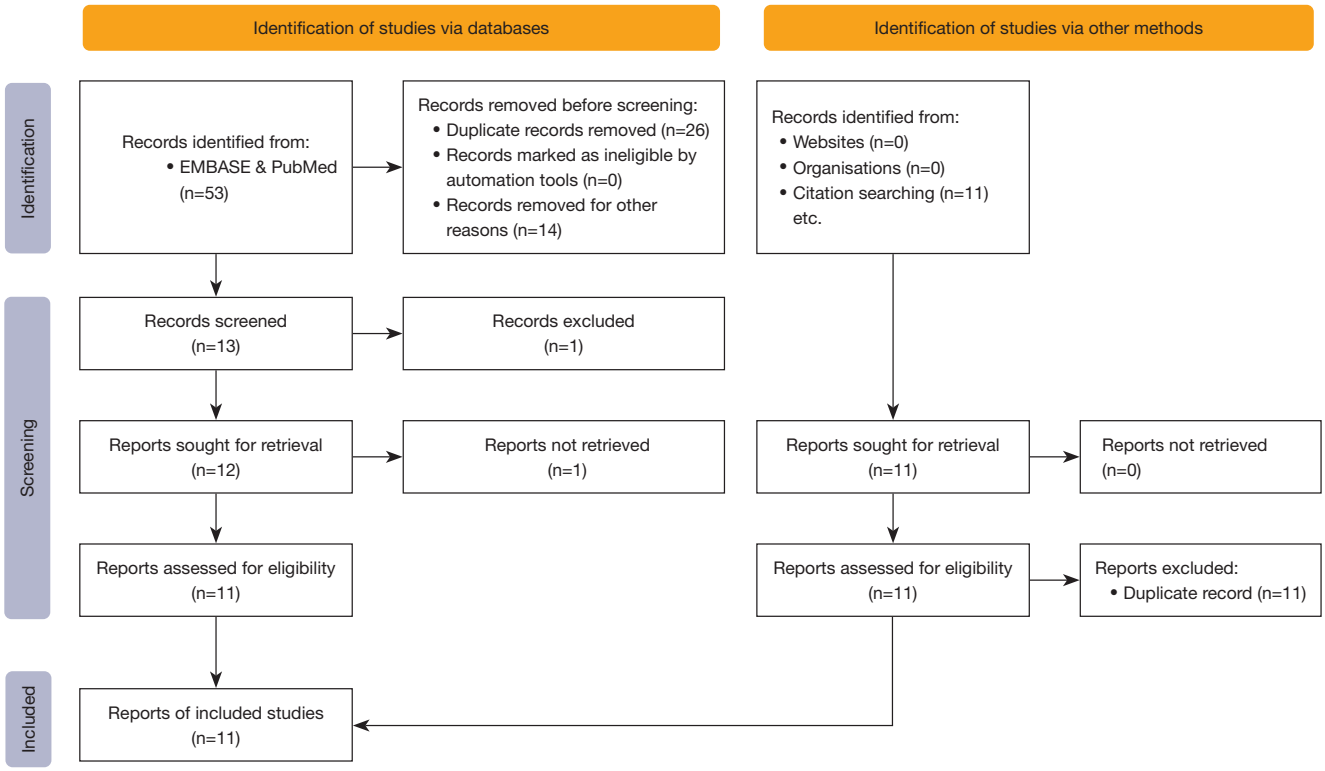

Figure 1 Flowchart describing systematic research search and study selection process.

surgical risk of patients; therefore, those measurements have not been included. The timing of HCM diagnosis was evaluated relative to TAVR procedure, with the diagnosis occurring pre-operatively, intra-operatively or post-operatively. HCM was diagnosed pre-operatively, intra-operatively and post-operatively in 27%, 55% and 18% respectively among the publications that reported timing. Although factors used to determine a HCM diagnosis by the authors varied, a left ventricle outflow tract (LVOT) mean gradient over 50 mmHg was a consistent and objective factor across all included reports. After patients were diagnosed and treated for HCM, 10 of 11 (90.9%) patients were discharged with no complications while 1 of 11 (9.1%) patients reported NYHA Class III symptoms after HCM treatment at 6-month follow-up. The all-cause mortality in our study population was 7.7% with a pacemaker implantation rate of 8.5% and vascular complication of 11.4% (*Table 2*).

Mhanna *et al.* reviewed the efficacy of TAVR in patients with HCM compared to SAVR, and found that after adjusting for comorbidities, TAVR had significantly lower rates of in-hospital mortality, bleeding requiring a blood transfusion, invasive mechanical ventilation, acute kidney injury, vascular complications, disposition to facility and decreased length of stay (LOS) compared to SAVR (5).

Bandyopadhyay *et al.* retrospectively reviewed the cases of 100,495 TAVR patients from the National Inpatient Sample databases from 2012 to 2016 to compare TAVR patients with HCM to those without HCM. The results of the review found that TAVR patients with HCM, when compared to the TAVR patients without HCM, were significantly more likely to be women and obese, along with a concomitant increased risk for acute kidney injury, aortic dissection, post-operative shock, and a higher risk for in-hospital mortality (6).

Discussion

SAVR was the traditional method of replacing severely stenotic aortic valves until clinical trials performed in the last decade demonstrated the increased utility of TAVR (2-4,21). Given the rapid increase in the TAVR procedures being performed, there is an urgent need for a review of outcomes for TAVR patients with various comorbidities. HCM presents a unique comorbidity for TAVR since the disease can present similarly to a stenotic aortic valve, only

Table 1 Summary of reviewed case reports and case studies

Author	No. of patients analyzed	Age (years) (averaged for case reviews)*	Sex	Valve type	Approach	STS score	Outcome	Timing of HCM diagnosis (relative to TAVR)	Alcohol septal ablation
Mhanna *et al.*, *Current Problems in Cardiology* (5)	595	79*	NA	NA	NA	NA	595 TAVR patients with HCM. 20 patients were in-hospital mortalities. No TAVR patients with HCM experienced a stroke, compared to 35 SAVR patients with HCM. 65 patients had new pacemaker implant	NA	Yes; 15 TAVR patients from the 595-patient cohort with HCM received ASA. No outcomes were specifically reported for the TAVR/ASA cohort
Bandyopadhyay *et al.*, *JAMA Netw Open* (6)	230	80.99*	F, 78.3%; M, 21.7%	NA	NA	NA	In-hospital mortality 18.6%. Pacemaker implant 2.3%	NA	NA
Olsen *et al.*, *J Med Case Rep* (12)	1	56	M	NA	Not reported	>8	Intraoperative heart failure after TAVR Alcohol septal ablation 8 months later	Intraoperative	Yes; 8 months post-TAVR
Shenouda *et al.*, *Curr Treat Options Cardiovasc Med* (13)	1	91	F	Edwards SAPIEN	Trans-femoral	Not reported	Unmasked LVOTO after TAVR. Patient expired 2 days after TAVR	Post-operative	Not reported
Shenouda *et al.*, *Curr Treat Options Cardiovasc Med* (13)	1	69	F	NA	Not reported	Not reported	Patient had ASA first. TAVR 3 months later with no complications	Pre-operative	Yes; 3 months post-TAVR
El-Sabawi *et al.*, *Catheter Cardiovasc Interv* (14)	1	90	F	Edwards SAPIEN 3	Not reported	Not reported	Discharged with no complication. NYHA Class I symptoms	Post-operative	Yes; immediately post-TAVR
El-Sabawi *et al.*, *Catheter Cardiovasc Interv* (14)	1	89	M	Edwards SAPIEN 3	Trans-apical	Not reported	Patient underwent ASA post TAVR but still exhibited Class III NYHA symptoms at six-month follow-up	Post-operative	Yes; 1-month post-TAVR
Suh *et al.*, *Catheter Cardiovasc Interv* (15)	1	82	F	Edwards SAPIEN	Trans-apical	Not reported	Patient was medically treated with intravenous fluids and beta-blockers. Patient was discharged to rehabilitation facility with no complications	Post-operative	None
Krishnaswamy *et al.*, *Circulation* (16)	1	91	F	23 mm Edwards SAPIEN	Trans-femoral	Not reported	Post-procedure septal alcohol ablation. At 1 month follow-up there was reduction of LVOT gradient	Intraoperative	Yes; immediately post-TAVR
Gerckens *et al.*, *J Invasive Cardiol* (17)	1	88	F	23 mm Edwards SAPIEN	Trans-femoral	7.0	Patient was given a septal alcohol ablation	Post-operative	Yes; 12 hours post-TAVR
Finkelstein *et al.*, *Catheter Cardiovasc Interv* (18)	1	91	F	23 mm CoreValve	Not reported	Not reported	No complications reported from patient	Pre-operative	None
Weich *et al.*, *JACC Case Rep* (19)	1	81	M	Edwards SAPIEN XT Size 29	Trans-femoral	2.8	6 weeks after valve replacement. A dual-chamber pacemaker system was implanted and the LVOT peak gradient resolved as of 3 weeks follow-up	Post-operative	None
Kitahara *et al.*, *Case Rep Cardiol* (20)	1	86	F	23 mm Edwards SAPIEN 3	Trans-femoral	9.8	Emergent ASA of the first proximal septal perforator artery reduced the gradient. 6-month follow-up did not reveal any complications	Pre-operative	Yes; immediately post-TAVR

*, case reviews with averaged age. NA, not available; F, female; M, male; STS, Society of Thoracic Surgeons; TAVR, transcatheter aortic valve replacement; HCM, hypertrophic cardiomyopathy; SAVR, surgical aortic valve replacement; LVOTO, left ventricular outflow tract obstruction; ASA, alcohol septal ablation; NYHA, New York Heart Association; LVOT, left ventricular outflow tract.

Table 2 Demographic, clinical and outcome characteristics of the study population (N=836)

Characteristic	Value
Age (years)	79.6±10
Gender (n=241)	
Male	53 [22]
Female	188 [78]
Access (n=7)	
Transfemoral	5 [71]
Transapical	2 [29]
Subclavian	0 [0]
Aortic valve gradient (mmHg) (n=9)	61.4±21.2
Type of valve (n=9)	
Edwards SAPIEN	8 [89]
CoreValve	1 [11]
Average Society of Thoracic Surgeons score (n=4)	6.9±3.0
Timing of HCM diagnosis with respect to TAVR (n=11)	
Preoperative	3 [27]
Intraoperative	6 [55]
Postoperative	2 [18]
Complications (n=836)	
All-cause mortality	64 [7.7]
Cardiogenic shock	83 [9.9]
Pacemaker placement	71 [8.5]
Vasopressors	31 [3.7]
Vascular complications	95 [11.4]
Alcohol septal ablation for HCM treatment (n=26)	
Yes	22 [84.6]
No	4 [15.4]

Data are presented as mean ± SD or n [%]. HCM, hypertrophic cardiomyopathy; TAVR, transcatheter aortic valve replacement; SD, standard deviation.

to be discovered after a new, fully functional aortic valve has been implanted in the patient. HCM can be fatal for the TAVR patient unless swift intervention is undertaken to reduce obstruction to cardiac output. Given the paucity of data regarding outcomes for TAVR patients with HCM, we performed this analysis to provide valuable insights.

The primary method of HCM diagnosis used in our study population was echocardiography. There was no noted difference in diagnosis or outcomes between trans-esophageal echocardiography and transthoracic echocardiography. An echocardiogram reveals three key diagnostic features of HCM such as septal anterior motion (SAM) of the mitral valve, LVOT gradient of over 50 mmHg or increased septal thickness. Majority of our reported patients were diagnosed with HCM intra-operatively during the TAVR procedure, and TAVR procedure led to unmasking on increased LVOT gradient. One of our reported cases presented with exertional dyspnea and angina of 1 year (14). Prior to TAVR, the patient did not have septal SAM of the mitral valve and a concentric myocardial hypertrophy of 19 mm. After TAVR, the patient was noted to have SAM of the mitral valve and a peak LVOT gradient of 55 mmHg on echo done at 1 month follow-up. After a septal alcohol ablation of the first proximal septal perforator artery, the patient still exhibited NYHA Class III symptoms at 6-month follow-up (14).

No conclusions can be drawn from the valve type used. It seems a vast majority of operators prefer the balloon expanding Edwards SAPIEN valve. Due to patients being diagnosed before, during and after the TAVR procedure with HCM, it is highly unlikely that the type of valve implanted plays any role in the development of dynamic left ventricular obstructions seen in HCM.

Favorable outcomes for TAVR patients with HCM include taking a thorough history and cardiac exam, specifically performing a standing Valsalva maneuver to separate the AS and HCM murmurs from each other during auscultation (22). A thorough pre-operative echocardiogram should look for asymmetric septal hypertrophy along with observance of any mid-ventricular cavitation or systolic anterior motion of the mitral valve indicating HCM. Following diagnosis, further studies are needed to establish the best course for HCM treatment, whether by medical therapy, alcohol septal ablation or surgery. Medical therapy includes intravenous (IV) fluid resuscitation and beta-blockers. Further research is also needed to determine if lowering the placement of the struts of the replacement aortic valve improves HCM symptoms, as suggested by Finkelstein *et al.* (18). Other authors suggest that placing the replacement valve too low may induce conduction problems that preclude this method of valve implantation. Alcohol septal ablation is the primary method of treating HCM and appears to provide no complications and rarely fails to treat HCM according to the papers in this review (13).

Limitations

Our study is a systematic review that addresses an important and underexplored clinical question but has inherent limitations because the primary data are from existing studies. There is significant heterogeneity in the included studies and the result of our analysis should be applied carefully in clinical practice. Further prospective and randomized controlled trials are needed to validate our findings.

Conclusions

TAVR patients with HCM are difficult to identify due to the similar clinical presentation of both AS and HCM. A thorough physical examination and detailed preoperative echocardiogram should look for SAM of the mitral valve, LVOT gradient of greater than 50 mmHg and increased septal thickness. Among TAVR patients diagnosed with HCM, alcohol septal ablation is a useful therapy that warrants more research.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-24-41/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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