





ORIGINAL RESEARCH



Patient-Specific Computer Simulation to Optimize Transcatheter Heart Valve Sizing and Positioning in Bicuspid Aortic Valve

Cameron Dowling, MBBS, PhD ^a, Robert Gooley, MBBS, PhD^a, Liam McCormick, MBBS, MD^a, Stephen J. Brecker, MD^b, Sami Firoozi, MBBS (Hons)^b, Vinayak N. Bapat, MBBS, MS^c, Susheel K. Kodali, MD^d, Omar K. Khalique, MD^d, Jorn Brouwer, MD ^e, and Martin J. Swaans, MD, PhD^e

^aMonashHeart, Monash Health and Monash Cardiovascular Research Centre, Monash University, Melbourne, Australia; ^bCardiology Clinical Academic Group, St. George's University of London and St. George's University Hospitals NHS Foundation Trust, London, UK; ^cCenter for Valve and Structural Heart Disease, Minneapolis Heart Institute, Minneapolis, Minnesota, USA; ^dColumbia Structural Heart and Valve Center, Columbia University Medical Center, New York, New York, USA; ^eDepartment of Cardiology, St. Antonius Hospital, Nieuwegein, The Netherlands

ABSTRACT

Background: Outcomes of transcatheter aortic valve replacement (TAVR) in bicuspid aortic valve (BAV) might be improved through better transcatheter heart valve (THV) sizing and positioning. Patient-specific computer simulation may be used to identify an optimal THV size and implant depth that minimizes paravalvular regurgitation. We sought to examine whether the usage of optimal THV sizing and positioning would be associated with improved clinical outcomes.

Methods: A multi-center retrospective study was performed on patients who had undergone TAVR in BAV. Finite element models of the aortic root were created and then finite element analysis was performed using different THV sizes and implant depths. Computational fluid dynamics was undertaken. Patients were classified as having optimal THV sizing and positioning if the predicted paravalvular regurgitation of the computer simulation corresponding to the implanted THV size and implant depth was within 5 mL/sec of the best possible computer simulation, and non-optimal if not. Clinical outcomes were compared between the two patient groups.

Results: A total of 50 patients were included in the study. Paravalvular regurgitation severity was higher in patients where non-optimal THV sizing and positioning was used ($P < 0.001$). At 2 years, the Kaplan-Meier estimate of the rate of death from any cause was higher in the group where non-optimal THV sizing and positioning was used (34.5% vs. 9.1%; hazard ratio, 6.23; 95% confidence interval, 1.04 to 37.44; $P = 0.02$ by log-rank test).

Conclusion: Computer simulation suggests that the usage of optimal THV sizing and positioning might improve clinical outcomes of TAVR in BAV.

Abbreviations: AUC: area under the receiver operating characteristic curve; BAV: bicuspid aortic valve; BAVi: bicuspid aortic valve imaging; CI: confidence interval; CPI: contact pressure index; CT: computed tomography; TAVR: transcatheter aortic valve replacement; THV: transcatheter heart valve

ARTICLE HISTORY Received 4 June 2021; Revised 20 August 2021; Accepted 30 September 2021

KEYWORDS Aortic valve stenosis; bicuspid aortic valve; computer simulation; finite element analysis; heart valve prosthesis implantation; transcatheter aortic valve replacement

Introduction

Transcatheter aortic valve replacement (TAVR) has been demonstrated in multiple randomized controlled trials to be associated with a lower risk of death and disabling stroke, when compared to surgery, independent of baseline surgical risk.¹ It is likely, therefore, that in time, TAVR will become the preferred treatment modality for the majority of patients with symptomatic severe tricuspid aortic valve stenosis, including those at low risk for surgery.

However, the majority of younger patients will have bicuspid aortic valve (BAV)² and this patient group has been excluded from all randomized controlled trials comparing TAVR and surgery. Therefore, in the absence of randomized data directly comparing these two treatment modalities,

careful patient selection by the Heart Team, based on clinical and perhaps more importantly, anatomical characteristics must remain paramount.

An emerging technology for assessing anatomical risk is patient-specific computer simulation. The technology has been retrospectively validated in both tricuspid³⁻⁵ and bicuspid aortic valves^{6,7} and prospective experience in both tricuspid⁸ and bicuspid aortic valves⁹ has recently been reported.

In this study we sought to investigate the role that patient-specific computer simulation might play in optimizing transcatheter heart valve (THV) sizing and positioning in BAV. Specifically, we hypothesized that clinical outcomes would be improved in patients where optimal THV sizing, as defined by



computer simulation, was used. Furthermore, we wished to use computer simulation to assess the differences in predicted paravalvular regurgitation between several different bicuspid sizing and positioning strategies.

Material and methods

A retrospective, multicentre study was performed on all bicuspid patients who underwent TAVR with the self-expanding Evolut R and Evolut PRO THVs (Medtronic, Minneapolis, Minnesota, USA) between August 2015 and November 2020. The study protocol was approved by a local research ethics committee and informed consent was deemed unnecessary.

Patient characteristics

Patient characteristics were obtained from the local electronic databases of the four participating study sites. National electronic records were reviewed in order to ascertain mortality status.

Cardiac computed tomography analysis

Cardiac computed tomography (CT) imaging was used to create aortic valve perpendicular plane and three-dimensional reconstructions with 3mensio Structural Heart version 9.1 (Pie Medical Imaging, Maastricht, Netherlands). Aortic valves were classified using the Sievers¹⁰ and TAVR-directed bicuspid aortic valve imaging (BAVi)¹¹ systems. Aortic root dimensions,¹² intercommissural distances¹³ and calcium volumes^{14,15} were recorded.

Computer simulation

Patient-specific computer simulation was performed using FEops HEARTguide technology (FEops NV, Ghent, Belgium) as has previously been described (Figure 1).^{6,16} Dedicated finite element models were developed for both Sievers Type 0 and Type 1 BAV. Computer simulation was performed with a THV based on perimeter-derived aortic annulus dimensions and further simulations were performed with a “downsized” THV. Computer simulation was performed at both a high (0 mm) and medium (4 mm) implant depth.

For each simulation, predicted paravalvular regurgitation in the left ventricular outflow tract was recorded.⁴ The sensitivity, specificity, positive predictive value and negative predictive value of the computer simulations were assessed using the simulation that most closely matched the implanted THV size and implant depth.

Predicted paravalvular regurgitation was compared using five different sizing and positioning strategies. The first two strategies used an annular-based THV sizing strategy, based on perimeter-derived aortic annular dimensions. This THV sizing strategy was assessed with the THV positioned at both a high and medium implant depth. The next two strategies used a supra-annular-based THV sizing strategy, based on both perimeter-derived aortic annular measurements and the intercommissural distance at 4 mm with selective downsizing in a tapered aortic root configuration.¹³ This THV sizing strategy was again assessed with the THV positioned at both a high and medium implant depth. Finally, a patient-specific THV sizing and positioning strategy was performed, which was based on the best computer simulation.

Clinical outcomes were compared between patients where optimal patient-specific THV sizing was used and those where it was not. Optimal patient-specific THV sizing and positioning

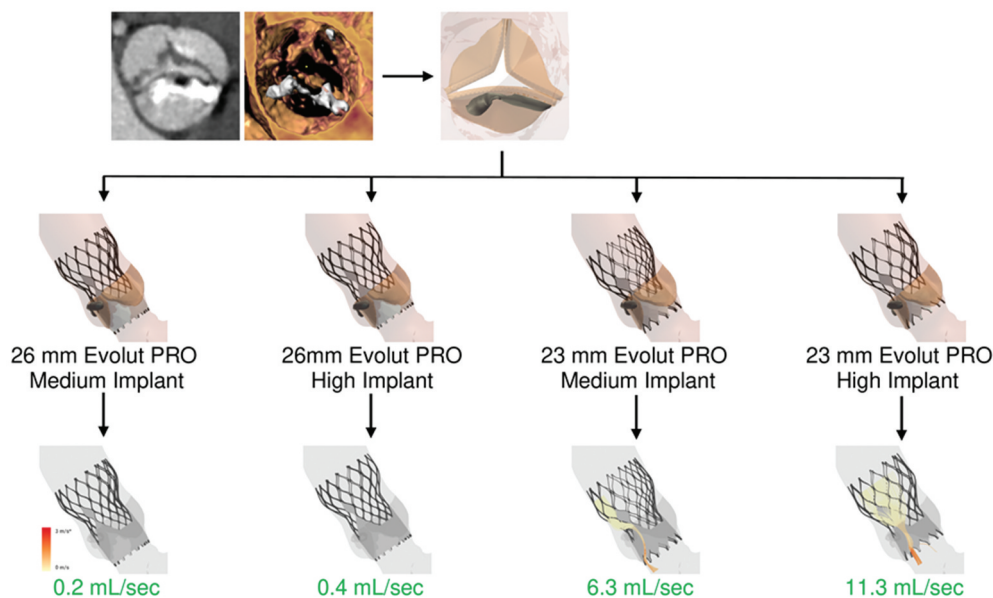


Figure 1. Patient-specific computer simulation. Pre-procedural cardiac computed tomography scans are used to create finite element models of the aortic root. The aortic wall, leaflets and calcium are modeled using different tissue characteristics. Finite element analysis is then performed with two different THV sizes, implanted at two different implant depths. Computational fluid dynamics analysis is undertaken to simulate paravalvular regurgitation for each of the four different THV sizing and positioning strategies. For this patient, the implantation of a 26 mm Evolut PRO THV, positioned at a medium implant depth, is associated with the lowest predicted paravalvular regurgitation.

was defined as a THV size and implant depth where predicted paravalvular regurgitation was within 5 mL/sec of the computer simulation which was associated with lowest predicted paravalvular regurgitation (Figure 2). Non-optimal patient-specific THV sizing and positioning was said to have occurred if the predicted paravalvular regurgitation was ≥ 5 mL/sec from the best possible computer simulation.

Procedural characteristics

TAVR procedural reports were reviewed, and characteristics recorded. TAVR procedural angiography was reviewed and implant depth defined as the distance from the base of the non-coronary cusp to the prosthesis inflow.¹⁷ Measurements were made using RadiAnt DICOM viewer version 2020.2 (Medixant, Poznan, Poland).

Echocardiographic assessment

Pre-procedural transthoracic echocardiograms were reviewed locally to assess left ventricular function, aortic valvular gradients and baseline aortic regurgitation severity. Post-procedure transthoracic echocardiograms were reviewed locally and paravalvular regurgitation severity assessed using a 5-class grading system.¹⁸

Statistical analysis

Statistical analysis was performed using SPSS version 26.0 (IBM Corporation, Armonk, New York, USA). Continuous variables are presented as mean \pm standard deviation and categorical variables as frequencies (percentage). The means of groups were compared with a two-tailed Student's t-test or analysis of variance where appropriate. Categorical variables

were compared with a Fisher's exact test or Chi-square test where appropriate. Discriminatory power was tested using the area under the receiver operating characteristic curve (AUC). Time-to-event analysis was performed with the use of Kaplan-Meier estimates and Cox regression and were compared with the use of the log-rank test.

Results

Baseline characteristics

A total of 50 patients were included in the study. The number of patients from each study site ranged from 2 to 27 patients. Baseline characteristics demonstrated an elderly population (mean age 78.0 ± 8.4 years) at increased risk for surgery (EuroScore II $5.5 \pm 5.1\%$) (Table 1).

Cardiac CT characteristics

Cardiac CT imaging demonstrated a wide variety of leaflet configurations, raphe locations and calcium distribution and there was strong visual agreement with the finite element computer models (Figure 3). The majority of patients had Sievers Type 1 BAV (86.0%) and a high proportion of patients had tricommissural valves (48.0%) when assessed using the TAVR-directed BAVi morphological classification system (Table 2). There was significant aortic calcium burden.

Computer simulation

The computer simulations demonstrated a discriminatory power to predict the development of \geq moderate paravalvular regurgitation (AUC, 0.87; 95% CI, 0.76 to 0.97; $P = 0.001$) (Figure 4). Using a previously defined cutoff of 13.5 mL/sec,⁶

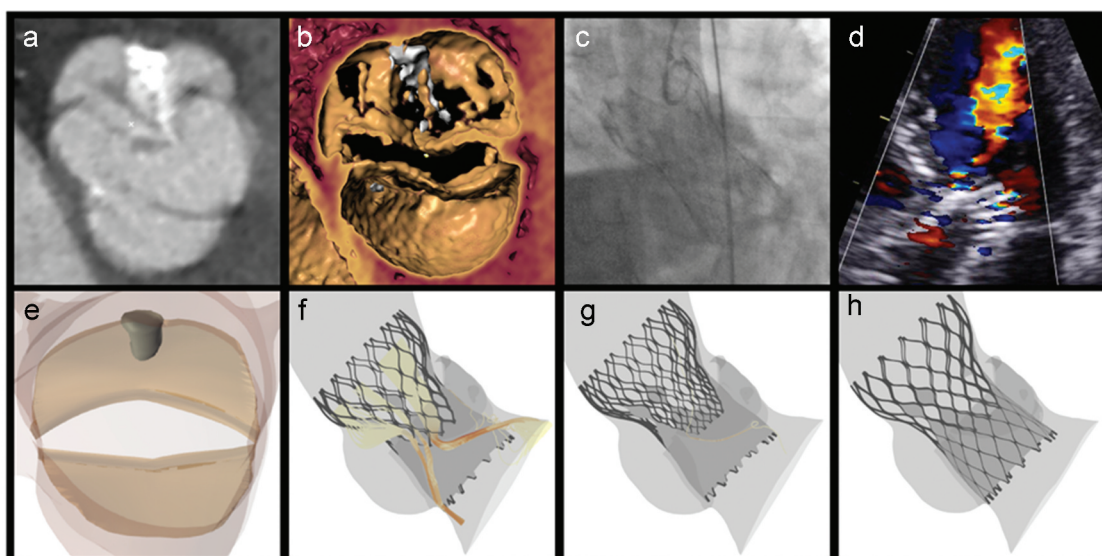


Figure 2. Patient-specific transcatheter heart valve sizing and positioning. (a-b) A patient with a Sievers Type 1 bicuspid aortic valve (c) underwent TAVR with a 29 mm Evolut PRO THV, (d) developing mild-to-moderate paravalvular regurgitation. (e) An example of the finite element model of the aortic root. (f) The computational fluid dynamics output of the computer simulation most closely matching the THV size and implant depth suggests that the patient will develop paravalvular regurgitation (predicated paravalvular regurgitation 11.4 mL/sec). Additional simulations suggest that implanting either a (g) 29 mm Evolut PRO (predicated paravalvular regurgitation 1.7 mL/sec) or a (h) 34 mm Evolut R THV (predicated paravalvular regurgitation 4.4 mL/sec) at a high implant depth might have reduced paravalvular regurgitation.

**Table 1.** Baseline patient characteristics.

Characteristic	n = 50
Age (yrs)	78.0 ± 8.4
Male	30 (60.0)
Body surface area (m ²)	1.78 ± 0.25
NYHA class III/IV	41 (82.0)
EuroSCORE II (%)	5.5 ± 5.1
Medical condition	
Diabetes mellitus	13 (26.0)
Creatinine clearance (ml/min/1.73 m ²)	58.4 ± 22.1
Chronic lung disease	12 (24.0)
Prior stroke or TIA	10 (20.0)
Peripheral vascular disease	4 (8.0)
Permanent pacemaker	8 (16.0)
Cardiac risk factors	
Prior CABG	5 (10.0)
Prior PCI	13 (26.0)
Prior balloon aortic valvuloplasty	2 (4.0)
Prior myocardial infarction	7 (14.0)
Prior atrial fibrillation or atrial flutter	15 (30.0)
Echocardiographic characteristics	
Peak aortic valve velocity (m/s)	4.24 ± 0.87
Mean aortic valve gradient (mm Hg)	47.1 ± 18.5
Aortic valve area (cm ²)	0.72 ± 0.20
Aortic regurgitation	
None	27 (54.0)
Mild	21 (42.0)
Moderate	2 (4.0)
Severe	0 (0.0)
Left ventricular ejection fraction (%)	50.4 ± 15.6

CABG denotes coronary artery bypass grafting, COPD chronic obstructive pulmonary disease, NYHA New York Heart Association, PCI percutaneous coronary intervention, and TIA transient ischemic attack.

a total of 16 patients were predicted to develop \geq moderate paravalvular regurgitation, representing a sensitivity of 88%, specificity of 79%, positive predictive value of 44%, negative predictive value of 97% and a diagnostic accuracy of 80%. Predicted paravalvular regurgitation was higher in patients who developed \geq moderate paravalvular regurgitation, when compared to patients who did not develop \geq moderate paravalvular regurgitation (26.7 ± 19.1 mL/sec vs. 7.8 ± 10.6 mL/sec; $P < 0.001$).

Optimal patient-specific THV sizing and positioning, as defined by computer simulation, was used in 39 patients (78.0%). In six (15.4%) of these patients, the CFD simulations predicted the development of \geq moderate paravalvular regurgitation.

Computer Simulation Assessment of THV Sizing and Positioning Strategies

An annular and supra-annular THV sizing strategy yielded the same THV size in 44 patients (88.0%). The predicted paravalvular regurgitation for an annular THV sizing algorithm was 10.3 ± 10.6 mL/sec when positioned at a high implant depth and 10.0 ± 12.1 mL/sec when positioned at a medium implant depth. The predicted paravalvular

regurgitation for the supra-annular THV sizing algorithm was 10.4 ± 10.6 mL/sec when positioned at a high implant depth and 10.1 ± 12.1 mL/sec when positioned at a medium implant depth. All four of these THV sizing and positioning strategies had similar predicted paravalvular regurgitation ($P = 0.64$) (Figure 5).

Patient-specific THV sizing and positioning was associated with lower predicted paravalvular regurgitation (7.0 ± 7.2 mL/sec) when compared to all four of the standardized THV sizing and positioning strategies (adjusted $P < 0.001$ for all comparisons).

For the six patients (12.0%) who had a tapered aortic root configuration, there was no difference in predicted paravalvular regurgitation between all four of the standardized THV sizing and positioning strategies ($P = 0.13$).

Procedural characteristics

TAVR procedures were mostly performed under local anesthesia and sedation (Table 3). There was a high usage of pre-dilatation (86.0%).

The mean THV implantation depth was 4.8 ± 3.0 mm, as measured at the non-coronary cusp. There was no difference in the THV implantation depth between patients in whom optimal and non-optimal THV and positioning was used (5.0 ± 3.4 mm vs. 4.8 ± 2.9 mm; $P = 0.86$).

THV migration was observed in 18.0%. Three patients (6.0%) required a second THV. In two patients of these there was aortic embolization of the THV on post-dilatation. The third patient had recurrent aortic and ventricular migration of the THV prior to release. The THV was removed and a smaller THV successfully implanted.

Echocardiographic outcomes

Echocardiographic outcomes are presented in Table 4. Moderate paravalvular regurgitation was developed in 16.0% of cases. Paravalvular regurgitation severity was higher in patients where non-optimal patient-specific THV sizing and positioning was used, when compared to those where non-optimal THV sizing and position was utilized ($P < 0.001$) (Figure 6). The incidence of \geq moderate paravalvular regurgitation was higher in patients where non-optimal THV sizing and positioning was used (45.5% vs. 7.7%; $P = 0.009$).

Long-term outcomes

Median follow-up was 13.6 months (interquartile range, 3.7 to 23.6 months). NYHA functional class information was available for 44 patients. At 30 days, NYHA functional class was similar amongst patients where optimal and non-optimal THV sizing and positioning was used ($P = 0.92$) (Figure 6).

At 2 years, non-optimal THV sizing and position was associated with a higher risk of death from any cause, when compared to optimal THV sizing and positioning (34.5% vs. 9.1%; hazard ratio, 6.23; 95% confidence interval, 1.04 to 37.44; $P = 0.02$ by log-rank test) (Figure 6).

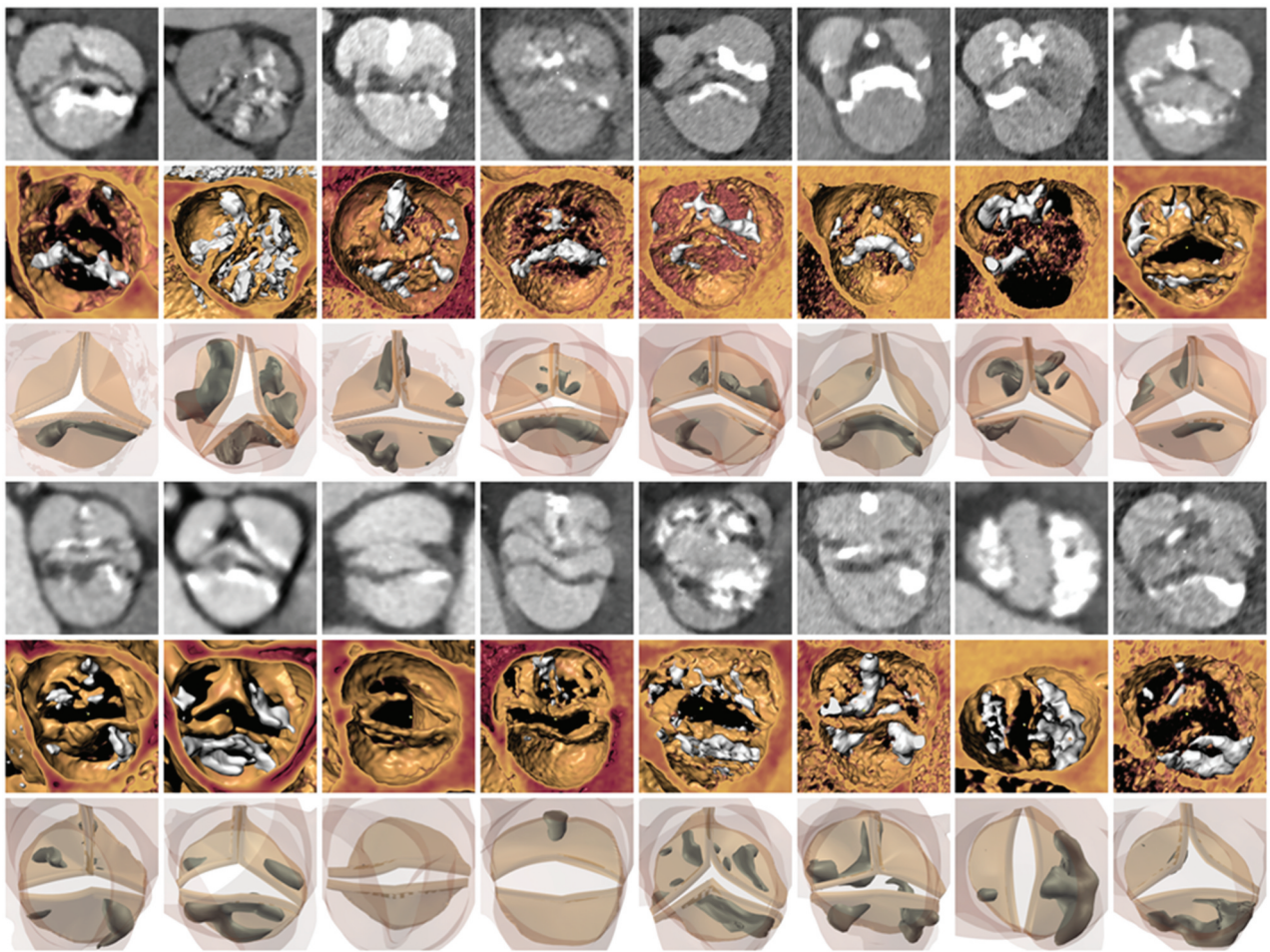


Figure 3. Aortic root cardiac CT imaging and computer models. There was strong visual agreement between the axial cardiac CT imaging, cardiac CT reconstructions and the finite element computer models of the aortic root.

Discussion

As TAVR continues to expand into younger, lower-risk patient cohorts, achieving excellent clinical outcomes in BAV is important. One potential strategy for improving outcomes of TAVR in BAV is through better THV sizing. Furthermore, outcomes of TAVR in BAV might also be enhanced through the usage of an optimal THV implantation depth.¹⁹

In this study we used pre-operative cardiac CT imaging to create patient-specific models of the aortic root that simulate important anatomical characteristics, including the aortic wall anatomy, aortic leaflet morphology and calcium distribution. Multiple computer simulations were then performed to identify a THV size and implant depth that minimized predicted paravalvular regurgitation.

We demonstrated, in a retrospective and observation manner, that patients where optimal THV sizing and positioning was used had improved clinical outcomes, when compared to patients where non-optimal THV sizing was employed. These clinical outcomes included reduced paravalvular regurgitation severity, reduced incidence of \geq moderate paravalvular regurgitation and improved long-term survival. These findings suggest that the usage of patient-specific computer simulation

to optimize THV sizing and positioning might improve clinical outcomes of TAVR in BAV.

Optimal THV sizing in BAV has yet to be established. Strategies include the usage of annular and supra-annular.^{13,20} sizing metrics. Furthermore, calcium volume, raphe length and raphe plane may also play an important role in BAV sizing.²¹⁻²³ Evidence to date suggests that clinical outcomes are similar between annular and supra-annular sizing strategies.²⁴⁻²⁶

In this study, we used computer simulation to evaluate predicted paravalvular regurgitation using a variety of THV sizing and positioning strategies. We demonstrated similar predicted paravalvular regurgitation between annular and supra-annular THV sizing strategies. Predicted paravalvular regurgitation was also similarly positioning the THV at a high and medium implant depth. We identified that patient-specific THV sizing and positioning were associated with reduced predicted paravalvular regurgitation when compared to all of these different THV sizing and positioning strategies, which supports our findings that optimal patient-specific THV sizing and positioning was associated with improved clinical outcomes.

In this study, the incidence of \geq moderate paravalvular regurgitation was high (16.0%), but nonetheless, consistent

**Table 2.** Cardiac CT Characteristics.

Characteristic	n = 50
Aortic valve morphology	
Sievers classification	
Sievers Type 0	7 (14.0)
Lateral	5 (10.0)
Antero-posterior	2 (4.0)
Sievers Type 1	43 (86.0)
Left-right raphe	34 (68.0)
Right-non raphe	8 (16.0)
Non-left raphe	1 (2.0)
TAVR-directed BAVi morphological classification	
Tricommissural	24 (48.0)
Coronary cusp fusion	20 (40.0)
Mixed cusp fusion	4 (8.0)
Bicommissural raphe type	19 (38.0)
Coronary cusp fusion	14 (28.0)
Mixed cusp fusion	5 (10.0)
Bicommissural non-raphe type	7 (14.0)
Coronary cusp fusion	2 (4.0)
Mixed cusp fusion	5 (10.0)
Left ventricular outflow tract diameter*	25.5 ± 3.3
Aortic annulus diameter*	25.6 ± 2.9
Sinus of Valsalva diameter*	35.2 ± 3.5
Sinotubular junction diameter*	31.0 ± 3.7
Ascending aorta diameter*	35.3 ± 4.1
Aortic leaflet calcium volume† (mm ³)	535.5 ± 443.3
Left ventricular outflow tract calcium†	19 (38.0)
Aortic valve calcium volume‡ (mm ³)	1087.7 ± 965.5

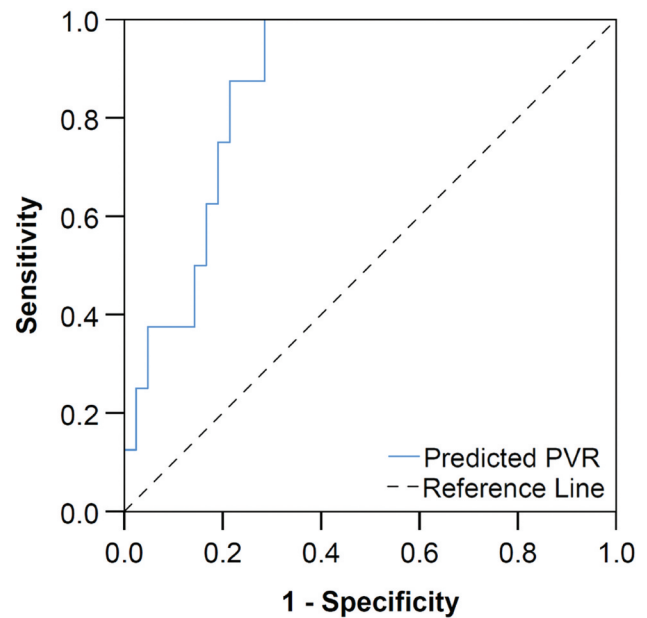
* Perimeter-derived values

† 850 Hounsfield unit threshold

‡ Luminal attenuation + 100 Hounsfield unit threshold

BAVi denotes bicuspid aortic valve imaging

with registry data of self-expanding THVs in bicuspid anatomy.²⁷ Furthermore, moderate paravalvular regurgitation developed in several patients (7.7%) where optimal THV sizing and positioning was used. Computer simulation may be used to identify BAV patients whose aortic root anatomy may not be favorable for TAVR, even when optimal THV sizing and positioning is utilized. These patients might be considered for treatment with surgery, especially if young and at low risk for surgery (Figure 7). This strategy of careful patient selection by the Heart Team, based on clinical and anatomical characteristics,

**Figure 4.** Receiver operating characteristics curve for the ability of the computer simulations to predict \geq moderate paravalvular regurgitation. The computer simulations demonstrated a discriminatory power to predict the development of \geq moderate paravalvular regurgitation.

PVR denotes paravalvular regurgitation.

has been recently demonstrated to be associated with favorable clinical outcomes in all patients.⁹

We undertook computer simulations targeting a high and medium THV implantation depth. THV migration was frequently observed in this study and in addition, a number of patients required a second THV prosthesis. Both BAV and self-expanding THVs are independent predictors for THV migration and embolization.²⁸ Furthermore, micro-dislodgement is common in self-expanding THVs.²⁹ The computer simulations are unable to predict these important procedural complications as the finite element analysis is not performed in a pressurized state. In addition, coaxial THV alignment may be challenging in bicuspid patients with an extremely horizontal aorta.³⁰ For these reasons, there may be some patients where it may not be feasible for operators to achieve a target implantation depth.

In this study, we chose to compare clinical outcomes between patients where optimal and non-optimal THV sizing

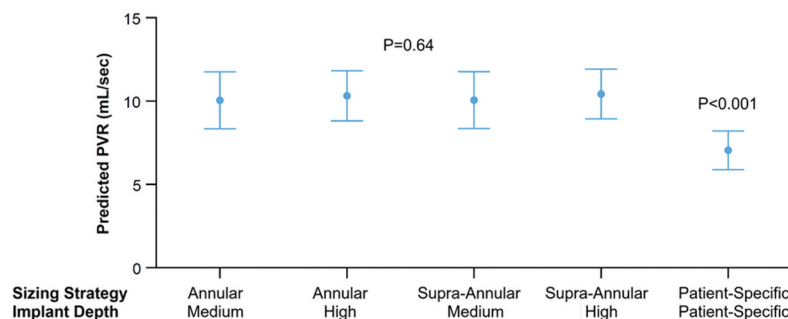
**Figure 5.** Computer assessment of THV sizing and positioning strategies. All four of the standardized THV sizing and positioning strategies are associated with a similar paravalvular regurgitation. Patient-specific THV sizing and positioning is associated with lower predicted paravalvular regurgitation when compared to all four of the standardized THV sizing and positioning algorithms.

Table 3. Procedural Characteristics.

Characteristic	n = 50
General anesthesia	19 (38.0)
Pre-dilatation	43 (86.0)
Transcatheter heart valve	
Evolut R	22 (44.0)
Evolut PRO	28 (56.0)
THV implantation depth	4.8 ± 3.0
Post-dilatation	23 (46.0)
THV migration	9 (18.0)
THV embolization	2 (4.0)
More than one THV inserted	3 (6.0)
Aortic annular rupture	1 (2.0)

THV denotes transcatheter heart valve.

Table 4. Echocardiographic Outcomes.

Outcome	n = 50
Peak velocity (m/s)	2.04 ± 0.55
Mean gradient (mm Hg)	9.4 ± 6.3
Effective orifice area (cm ²)	1.90 ± 0.44
Paravalvular regurgitation severity	
None	8 (16.0)
Trace	17 (34.0)
Mild	13 (26.0)
Mild-to-moderate	4 (8.0)
Moderate	8 (16.0)
Moderate-to-severe	0 (0.0)
Severe	0 (0.0)

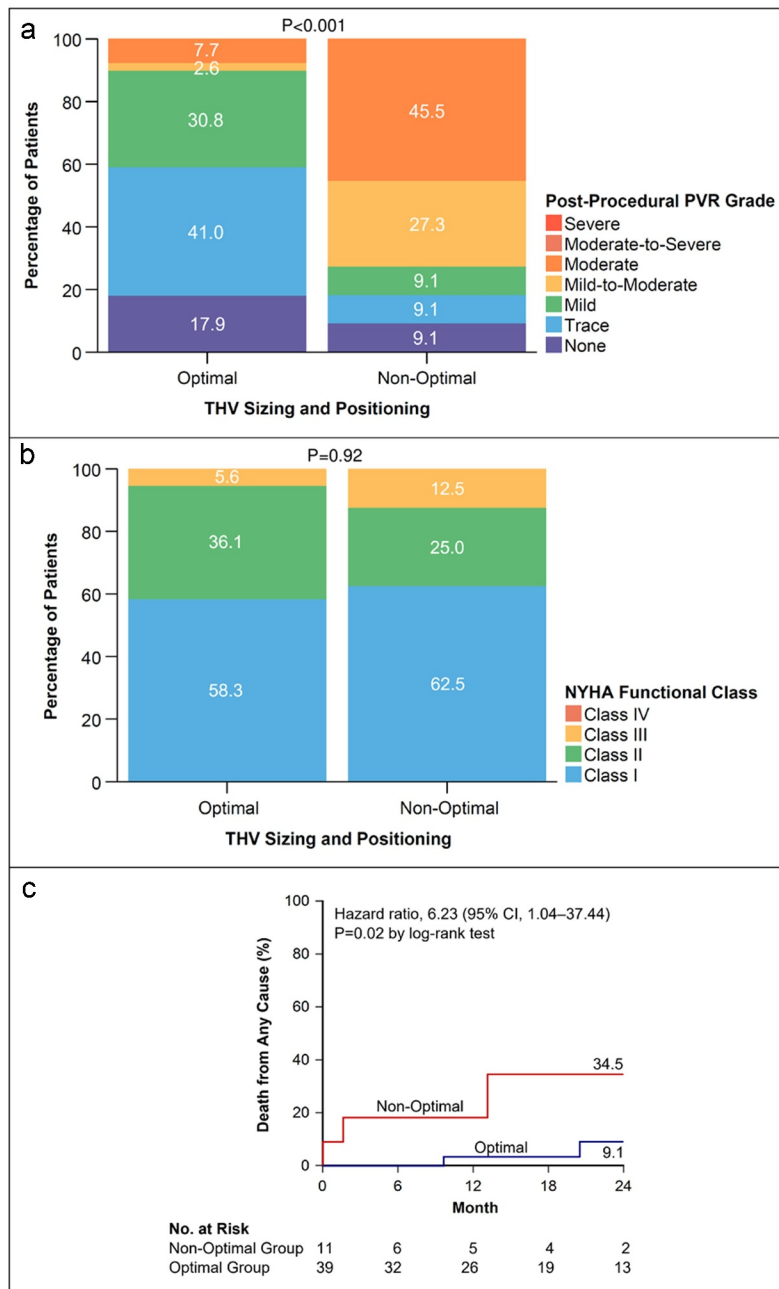


Figure 6. Clinical outcomes. (a) Comparisons of post-procedural paravalvular regurgitation severity. Post-procedural paravalvular regurgitation severity was higher in patients where non-optimal transcatheter heart valve sizing and positioning was used, when compared to patients where optimal sizing and positioning was employed. (b) New York Heart Association Functional Class. At 30-days, NYHA Functional Class was similar between the two patient groups. (c) Time-to-Event Curves for Death from Any Cause. The risk of death was higher in patients where non-optimal THV sizing and positioning was used. NYHA denotes New York Heart Association, and THV transcatheter heart valve.

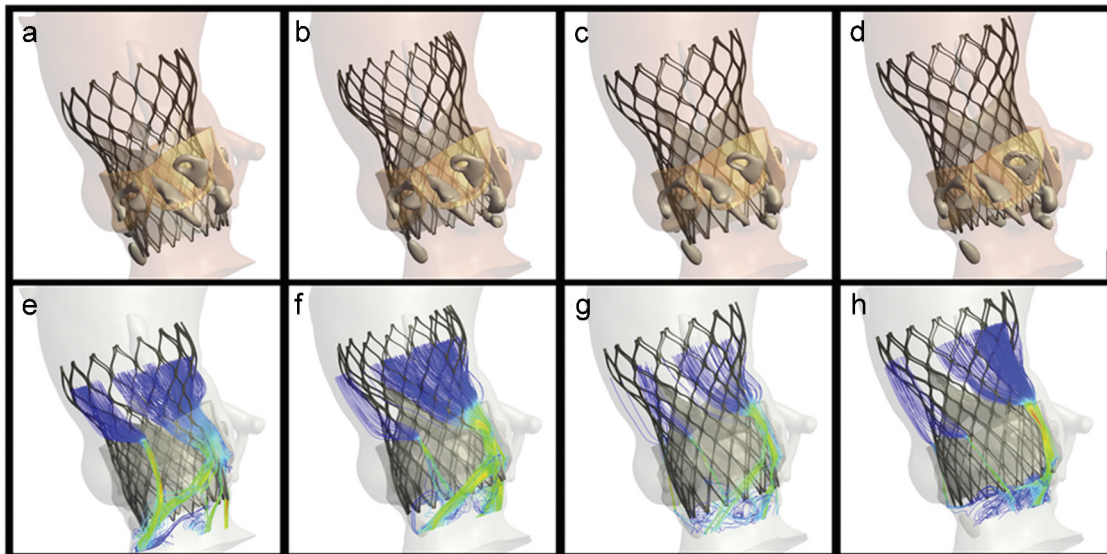


Figure 7. Computer simulations on a patient with potentially unfavorable aortic root anatomy for TAVR with a self-expanding THV. Finite element analysis has been performed with a 29 mm Evolut PRO (a, b) and a 34 mm Evolut R (c, d) THV, positioned at both a medium (a, c) and high (b, d) implantation depth. All computational fluid dynamics simulations predict the development of \geq moderate paravalvular regurgitation.

and positioning was employed and used a cutoff of 5 mL/sec from the computer simulation with the lowest predicated paravalvular regurgitation. We chose this threshold as it was felt that small differences in predicted paravalvular regurgitation (<5 mL/sec) would be unlikely to alter operator decision-making processes. This is consistent with results from the TAVIguide study, where in only 12% of cases the implantation depth altered to minimize predicted paravalvular regurgitation.⁸

Ideally, all BAV patients would receive patient-specific computer simulation. However, due to time and financial constraints, this technology might be selectively used for patients with adverse anatomical features such as a calcified raphe or excess leaflet calcification.³¹ Furthermore, this technology may selectively be used for patients with a tapered aortic root configuration, where ambiguity in THV sizing may arise.

Our study only evaluated paravalvular regurgitation and would be strengthened through the evaluation of conduction disturbance, as the incidence of permanent pacemaker implantation is higher in patients with BAV, when compared to patients with tricuspid aortic valve,³² and the usage of patient-specific techniques has recently been demonstrated to reduce the incidence of this complication.^{17,33}

Valve hemodynamics are an important consideration in BAV patients, as THV gradients are higher in patients in BAV, when compared to patients with tricuspid aortic valve.³⁴ Furthermore, hemodynamic profiles are less favorable for TAVR in Sievers Type 0 BAV, when compared to TAVR in Sievers Type 1 BAV.³⁵ The role of computer simulation in predicting THV hemodynamic profiles should be examined in future studies.

Finally, aortic root injury is more common in patients with BAV when compared to patients with tricuspid aortic valve,³² and in this study, aortic annular rupture developed in one

patient. The computer simulations are currently unable to model this important procedural complication.

Limitations



This was a small, retrospective and observational study, and our findings should be considered hypothesis generating. Further prospective investigation in a large cohort is required to definitively evaluate the role of this technology within the BAV cohort. Whilst the computer simulations model pre-dilatation, post-dilatation is not accounted for within the finite element analysis process, and this may, in part, explain the modest positive predictive value (44%) of the computer simulations, and could potentially limit the clinical utility of this technology. In this study 44% of patients received second-generation Evolut R devices. Additional validation is required with current-generation Evolut PRO self-expanding THVs, which have been demonstrated to be associated with favorable clinical outcomes.^{26,36} Furthermore, validation is also required with balloon-expandable and mechanically expanding THVs. In addition, in this study, some unmeasured patient selection bias may have occurred, because operators may have chosen to predominantly use balloon-expandable devices for the treatment of bicuspid patients, as these devices have been associated with a lower incidence of \geq moderate paravalvular regurgitation in bicuspid anatomy.²⁷ Our study assessed paravalvular regurgitation severity locally and would be strengthened through the addition of a centralized echocardiographic core laboratory. THV implantation depth was assessed using procedural angiography, which could potentially introduce parallax errors,³⁷ and our study would be improved through the usage of systematic post-procedural CT imaging.



Conclusion

Computer simulation suggests that the usage of optimal THV sizing and positioning might improve clinical outcomes of TAVR in BAV.

ORCID

Cameron Dowling  <http://orcid.org/0000-0003-3191-5361>
 Jorn Brouwer  <http://orcid.org/0000-0002-7815-1031>

Funding

This study is part of a project that has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No. 945698.

Disclosure statement

Dr. Dowling reports grants from Medtronic, outside the submitted work. A/Prof. Gooley reports personal fees from Boston Scientific, outside the submitted work. Dr. McCormick reports personal fees from Boston Scientific, outside the submitted work. Prof. Brecker reports grants and personal fees from Medtronic, outside the submitted work. Dr. Swaans reports personal fees from Abbott Vascular, Boston Scientific, Philips Healthcare and BioVentrix, outside the submitted work. All other authors have nothing to disclose.

References

- Dowling C, Kondapally Seshasai SR, Firoozi S, Brecker SJ. Transcatheter aortic valve replacement versus surgery for symptomatic severe aortic stenosis: a reconstructed individual patient data meta-analysis. *Catheter Cardiovasc Interv.* 2020;96(1):158–166. doi:10.1002/ccd.28504.
- Roberts WC, Ko JM. Frequency by decades of unicuspid, bicuspid, and tricuspid aortic valves in adults having isolated aortic valve replacement for aortic stenosis, with or without associated aortic regurgitation. *Circulation.* 2005;111(7):920–925. doi:10.1161/01.CIR.0000155623.48408.C5.
- Schultz C, Rodriguez-Olivares R, Bosmans J, et al. Patient-specific image-based computer simulation for the prediction of valve morphology and calcium displacement after TAVI with the Medtronic CoreValve and the Edwards SAPIEN valve. *EuroIntervention.* 2016;11(9):1044–1052. doi:10.4244/EIJV11I9A212.
- de Jaegere P, De Santis G, Rodriguez-Olivares R, et al. Patient-specific computer modeling to predict aortic regurgitation after transcatheter aortic valve replacement. *JACC Cardiovasc Interv.* 2016;9:508–512.
- Rocatello G, El Faquir N, De Santis G, et al. Patient-specific computer simulation to elucidate the role of contact pressure in the development of new conduction abnormalities after catheter-based implantation of a self-expanding aortic valve. *Circ Cardiovasc Interv.* 2018;11(2):e005344. doi:10.1161/CIRCINTERVENTIONS.117.005344.
- Dowling C, Bavo AM, El Faquir N, et al. Patient-specific computer simulation of transcatheter aortic valve replacement in bicuspid aortic valve morphology. *Circ Cardiovasc Imaging.* 2019;12:e009178.
- Brouwer J, Gheorge L, Nijenhuis VJ, et al. Insight on patient specific computer modeling of transcatheter aortic valve implantation in patients with bicuspid aortic valve disease. *Catheter Cardiovasc Interv.* 2019;93(6):1097–1105. doi:10.1002/ccd.27990.
- El Faquir N, De Backer O, Bosmans J, et al. Patient-specific computer simulation in TAVR with the self-expanding Evolut R valve. *JACC Cardiovasc Interv.* 2020;13(15):1803–1812. doi:10.1016/j.jcin.2020.04.018.
- Dowling C, Firoozi S, Brecker SJ. First-in-human experience with patient-specific computer simulation of TAVR in bicuspid aortic valve morphology. *JACC Cardiovasc Interv.* 2020;13(2):184–192. doi:10.1016/j.jcin.2019.07.032.
- Sievers HH, Schmidtke C. A classification system for the bicuspid aortic valve from 304 surgical specimens. *J Thorac Cardiovasc Surg.* 2007;133(5):1226–1233. doi:10.1016/j.jtcvs.2007.01.039.
- Jilaihawi H, Chen M, Webb J, et al. A bicuspid aortic valve imaging classification for the TAVR era. *JACC Cardiovasc Imaging.* 2016;9(10):1145–1158. doi:10.1016/j.jcmg.2015.12.022.
- Buellesfeld L, Stortecky S, Kalesan B, et al. Aortic root dimensions among patients with severe aortic stenosis undergoing transcatheter aortic valve replacement. *JACC Cardiovasc Interv.* 2013;6(1):72–83. doi:10.1016/j.jcin.2012.09.007.
- Tchetche D, de Biase C, van Gils L, et al. Bicuspid aortic valve anatomy and relationship with devices: the BAVARD multicenter registry. *Circ Cardiovasc Interv.* 2019;12(1):e007107. doi:10.1161/CIRCINTERVENTIONS.118.007107.
- Jilaihawi H, Makkar RR, Kashif M, et al. A revised methodology for aortic-valvar complex calcium quantification for transcatheter aortic valve implantation. *Eur Heart J Cardiovasc Imaging.* 2014;15(12):1324–1332. doi:10.1093/ehjci/jeu162.
- Bettinger N, Khalique OK, Krepp JM, et al. Practical determination of aortic valve calcium volume score on contrast-enhanced computed tomography prior to transcatheter aortic valve replacement and impact on paravalvular regurgitation: elucidating optimal threshold cutoffs. *J Cardiovasc Comput Tomogr.* 2017;11(4):302–308. doi:10.1016/j.jcct.2017.04.009.
- Dowling C, Gooley R, McCormick L, Firoozi S, Brecker SJ. Patient-specific computer simulation: an emerging technology for guiding the transcatheter treatment of patients with bicuspid aortic valve. *Interv Cardiol.* 2021;16:e26. doi:10.15420/icr.2021.09.
- Jilaihawi H, Zhao Z, Du R, et al. Minimizing permanent pacemaker following repositionable self-expanding transcatheter aortic valve replacement. *JACC Cardiovasc Interv.* 2019;12(18):1796–1807. doi:10.1016/j.jcin.2019.05.056.
- Pibarot P, Hahn RT, Weissman NJ, Monaghan MJ. Assessment of paravalvular regurgitation following TAVR: a proposal of unifying grading scheme. *JACC Cardiovasc Imaging.* 2015;8(3):340–360. doi:10.1016/j.jcmg.2015.01.008.
- Blackman D, Gabbieri D, Del Blanco BG, et al. Expert consensus on sizing and positioning of SAPIEN 3/ultra in bicuspid aortic valves. *Cardiol Ther.* 2021. doi:10.1007/s40119-021-00223-9.
- De Biase C, Agudze E, Siddiqui S, et al. Supra-annular sizing for prediction of THV expansion in bicuspid aortic valves: a MSCST study. *Struct Heart.* 2021;5(4):382–391. doi:10.1080/24748706.2021.1915515.
- Petronio AS, Angelillis M, De Backer O, et al. Bicuspid aortic valve sizing for transcatheter aortic valve implantation: development and validation of an algorithm based on multi-slice computed tomography. *J Cardiovasc Comput Tomogr.* 2020;14(5):452–461. doi:10.1016/j.jcct.2020.01.007.
- Iannopolo G, Romano V, Buzzatti N, et al. A novel supra-annular plane to predict TAVI prosthesis anchoring in raphe-type bicuspid aortic valve disease: the LIRA plane. *EuroIntervention.* 2020;16(3):259–261. doi:10.4244/EIJ-D-19-00951.
- Iannopolo G, Romano V, Buzzatti N, et al. Supra-annular sizing of transcatheter aortic valve prostheses in raphe-type bicuspid aortic valve disease: the LIRA method. *Int J Cardiol.* 2020;317:144–151. doi:10.1016/j.ijcard.2020.05.076.
- Kim WK, Renker M, Rolf A, et al. Annular versus supra-annular sizing for TAVI in bicuspid aortic valve stenosis. *EuroIntervention.* 2019;15(3):e231–e238. doi:10.4244/EIJ-D-19-00236.
- Weir-McCall JR, Attinger-Toller A, Blanke P, et al. Annular versus supra-annular sizing for transcatheter aortic valve replacement in bicuspid aortic valve disease. *J Cardiovasc Comput Tomogr.* 2020;14(5):407–413. doi:10.1016/j.jcct.2020.01.008.



26. Tchetché D. Transcatheter treatment of bicuspid aortic valves with the Evolut platform: the BIVOLUT-X registry. Presented on: June 27, 2020. PCR e-Course; 2020.
27. Mangieri A, Tchetché D, Kim WK, et al. Balloon versus self-expandable valve for the treatment of bicuspid aortic valve stenosis: insights from the BEAT international collaborative registries. *Circ Cardiovasc Interv.* 2020;13(7):e008714. doi:10.1161/CIRCINTERVENTIONS.119.008714.
28. Kim WK, Schäfer U, Tchetché D, et al. Incidence and outcome of peri-procedural transcatheter heart valve embolization and migration: the TRAVEL registry (TranscatheteR HeArt Valve EmboLization and Migration). *Eur Heart J.* 2019;40(38):3156–3165. doi:10.1093/eurheartj/ehz429.
29. Hellhammer K, Piayda K, Afzal S, et al. Micro-dislodgement during transcatheter aortic valve implantation with a contemporary self-expandable prosthesis. *PLoS One.* 2019;14(11):e0224815. doi:10.1371/journal.pone.0224815.
30. Gunasekaran S, Ganesapandi R, Sivaprakasam MC. Transfemoral transcatheter aortic valve implantation in bicuspid aortic valve with extreme horizontal aorta to left ventricle angulation challenges. *IHJ Cardiovascular Case Rep. (CVCR).* 2018;2:S54–S56. doi:10.1016/j.ihjccr.2018.08.001.
31. Yoon SH, Kim WK, Dhoble A, et al. Bicuspid aortic valve morphology and outcomes after transcatheter aortic valve replacement. *J Am Coll Cardiol.* 2020;76(9):1018–1030. doi:10.1016/j.jacc.2020.07.005.
32. Makkar RR, Yoon SH, Leon MB, et al. Association between transcatheter aortic valve replacement for bicuspid vs tricuspid aortic stenosis and mortality or stroke. *Jama.* 2019;321(22):2193–2202. doi:10.1001/jama.2019.7108.
33. Ben-Shoshan J, Alosaimi H, Lauzier PT, et al. Double S-curve versus cusp-overlap technique: defining the optimal fluoroscopic projection for TAVR with a self-expanding device. *JACC Cardiovasc Interv.* 2021;14(2):185–194. doi:10.1016/j.jcin.2020.10.033.
34. Forrest JK, Kaple RK, Ramlawi B, et al. Transcatheter aortic valve replacement in bicuspid versus tricuspid aortic valves from the STS/ACC TVT registry. *JACC Cardiovasc Interv.* 2020;13(15):1749–1759. doi:10.1016/j.jcin.2020.03.022.
35. Kumar K, Simpson TF, Akhavein R, et al. Hemodynamic and conduction system outcomes in Sievers Type 0 and Sievers Type 1 bicuspid aortic valves post transcatheter aortic valve replacement. *Struct Heart.* 2021;5(3):287–294. doi:10.1080/24748706.2021.1883782.
36. Forrest JK, Ramlawi B, Deeb GM, et al. Transcatheter aortic valve replacement in low-risk patients with bicuspid aortic valve stenosis. *JAMA Cardiol.* 2021;6:50–57.
37. Thériault-Lauzier P, Andalib A, Martucci G, et al. Fluoroscopic anatomy of left-sided heart structures for transcatheter interventions: insight from multislice computed tomography. *JACC Cardiovasc Interv.* 2014;7:947–957.