Patient-specific Computer Simulation: An Emerging Technology for Guiding the Transcatheter Treatment of Patients with Bicuspid Aortic Valve

Cameron Dowling ⓘ,[1] Robert Gooley,[1] Liam McCormick,[1] Sami Firoozi[2] and Stephen J Brecker[2]

1. MonashHeart, Monash Health and Monash Cardiovascular Research Centre, Monash University, Melbourne, Australia;
2. Cardiology Clinical Academic Group, St George's, University of London and St George's University Hospitals
NHS Foundation Trust, London, UK

Abstract

Transcatheter aortic valve implantation (TAVI) is increasingly being used to treat younger, lower-risk patients, many of whom have bicuspid aortic valve (BAV). As TAVI begins to enter these younger patient cohorts, it is critical that clinical outcomes from TAVI in BAV are matched to those achieved by surgery. Therefore, the identification of patients who, on an anatomical basis, may not be suitable for TAVI, would be desirable. Furthermore, clinical outcomes of TAVI in BAV might be improved through improved transcatheter heart valve sizing and positioning. One potential solution to these challenges is patient-specific computer simulation. This review presents the methodology and clinical evidence surrounding patient-specific computer simulation of TAVI in BAV.

Transcatheter aortic valve implantation (TAVI) has been demonstrated in randomised trials to be associated with a lower risk of death and disabling stroke compared with surgery.[1] Therefore, it is likely that TAVI will increasingly become the preferred treatment modality for most patients with symptomatic severe aortic stenosis, regardless of baseline surgical risk. However, as TAVI begins to enter younger, lower-risk cohorts, the prevalence of bicuspid aortic valve (BAV) will increase, and it is important that clinicians recognise that this patient subset was excluded from all clinical trials comparing TAVI and surgery.[2] Although clinical outcomes of TAVI in BAV have improved with newer generation devices, the incidence of paravalvular regurgitation and of conduction disturbance remains higher than with surgery, and both of these complications have been associated with adverse long-term outcomes.[3–6]

Therefore, in the absence of randomised 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. Furthermore, optimising transcatheter heart valve (THV) sizing and positioning within bicuspid anatomy remains an important consideration.

With this as a background, one potential solution to the challenges of TAVI in BAV is patient-specific computer simulation. In this review, we discuss how patient-specific computer simulation may be used to guide the transcatheter treatment of patients with BAV.

Patient-specific Computer Simulation

Patient-specific computer simulation is a method of simulating the interaction between a device and the native anatomy.[7] The simulations use the geometric and mechanical properties of both the device and patient anatomy to predict the deformation of the device and the potential for important procedural complications. The technology has been studied in a number of structural heart procedures, including TAVI, left atrial appendage occlusion and transcatheter mitral valve replacement.[8–20]

Patient-specific computer simulation of TAVI in BAV has been undertaken in a number of small studies, but the largest validation and prospective clinical experience has been performed using the FEops HEARTguide technology.[11,12,21–25] An overview of patient-specific computer simulation of TAVI in BAV is presented in *Figure 1*.
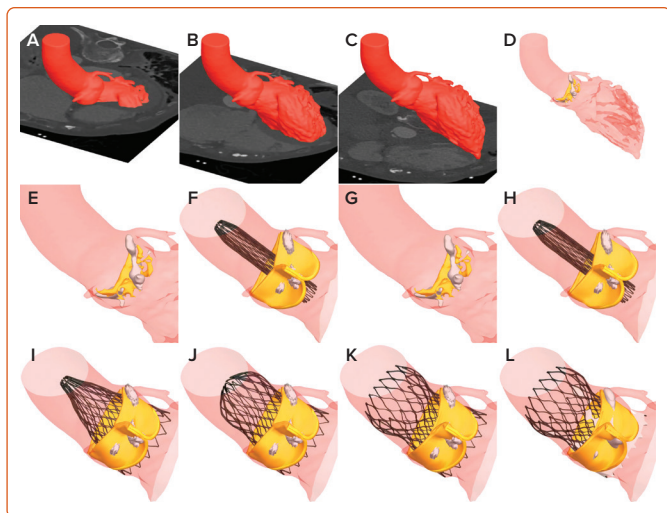
Finite Element Analysis

The first step in patient-specific computer simulation is to create a finite element model of the aortic root (*Figure 2 and Supplementary Material Video 1*). Pre-procedural cardiac CT imaging is segmented with inclusion of the left ventricular outflow tract, aortic root and the ascending aorta.

Figure 1: Patient-specific Computer Simulation of Transcatheter Aortic Valve Implantation in Bicuspid Aortic Valve
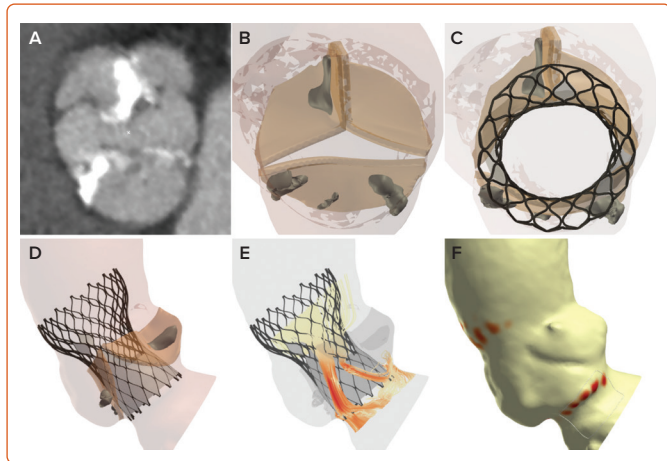
A and B: Pre-procedural cardiac CT imaging (A) is used to create a finite element model (B) of the aortic root. C,D: Finite element analysis is performed to simulate the interaction between the transcatheter heart valve and the native anatomy. E: The blood domain is extracted and computational fluid dynamics is used to simulate paravalvular regurgitation. F: The force exerted by the transcatheter heart valve on the left bundle branch is measured and used to simulate conduction disturbance.

Figure 2: Finite Element Analysis

A–C: Pre-procedural cardiac CT imaging is used to create a finite element model of the aortic root. D,E: The aortic wall, leaflets and calcium are given different mechanical characteristics. F–L: Finite element analysis is performed to simulate the interaction between the transcatheter heart valve and the native anatomy.

The aortic root tissues, leaflets and calcification are modelled with different elastic material properties.[13,26] These material characteristics were derived through a process of iterative back-calculation from 39 tricuspid aortic valve patients who had pre- and post-procedural cardiac CT.[15] Aortic leaflet modelling has been developed for both Sievers type 0 and type 1 BAV.[27] Furthermore, modelling can be performed to reflect both tricommissural, bicommissural raphe-type and bicommissural non-raphe-type leaflet morphology.[28]

Finite element models have been developed for a number of THVs, including SAPIEN XT (Edwards Lifesciences), CoreValve, Evolut R, Evolut PRO, Evolut PRO+ (Medtronic), Lotus and ACURATE neo (Boston Scientific). The frame morphology is derived from micro-CT, or based on information shared by the device manufacturer. The strut width is obtained from optical microscopy, or again, based on information shared by the

manufacturer. Mechanical properties of the nickel titanium (Nitinol) frames are obtained through *in vitro* radial compression testing, with radial force recorded throughout the compression and unloading cycle.

Pre-dilatation is simulated and then the finite element model of the THV is positioned within the aortic root model. Finite element analysis (FEA) is performed to simulate the interaction between the THV and the native anatomy.

Computational Fluid Dynamics

An overview of the computational fluid dynamics (CFD) is presented in *Figure 3*. The blood domain is first extracted from the FEA output. A fixed pressure gradient of 32 mmHg is applied across the aortic root, a value that was derived using invasive measurement from 60 patients with tricuspid aortic valve.[14] CFD is performed and paravalvular regurgitation is recorded in the left ventricular outflow tract. Importantly, the CFD simulations do not model for valvular regurgitation. The simulations are performed with the bioprosthetic leaflets aligned with the native leaflets, given that non-alignment of the bioprosthetic leaflets has been demonstrated to have minimal impact on the computer simulation output.[16]

Conduction Disturbance Modelling

Conduction disturbance modelling is presented in *Figure 4*. The inferior border of the membranous septum is located and then a region extending to 15 mm below the aortic annulus is identified. This anatomical region of interest is a surrogate for the His bundle and proximal left bundle branch.[29] The force exerted by the THV on the native anatomy is extracted from the FEA modelling. The percentage of the region of interest that is subject to pressure (contact pressure index) is recorded. Importantly, the simulations do not account for differences in THV frame rotation, given that this has been demonstrated to have minimal impact on the computer simulation output.[13]

Validation of Computer Simulations

Retrospective validation of the computer simulations has been performed in 37 patients who had pre- and post-procedural cardiac CT imaging, with further validation performed on seven patients who had peri-procedural transoesophageal imaging.[9,12] The majority of these patients had Sievers type 1 BAV (82%). The FEA simulations were found to be reliable at predicting the THV frame deformation within the bicuspid anatomy.

Validation of the CFD analysis has demonstrated that the simulations are reliable at predicting the development of moderate paravalvular regurgitation. A predicted paravalvular regurgitation of 13.6 ml/s was found to be 92% sensitive and 72% specific for predicting the development of moderate paravalvular regurgitation, representing a positive predictive value of 61% and a negative predictive value of 95%.

Limited validation of the conduction disturbance modelling has been performed in 20 patients. A contact pressure index of 0.14 was found to have a sensitivity of 67% and a specificity of 72% for predicting the development of major conduction abnormalities (new left bundle branch block, Mobitz type II second-degree atrioventricular block or third-degree atrioventricular block), representing a positive predictive value of 100% and a negative predictive value of 50%.

## Optimising Transcatheter Heart Valve Sizing and Positioning

The computer simulations may be used to optimise THV sizing and positioning to reduce the severity of predicted paravalvular regurgitation

Figure 3: Computational Fluid Dynamics Simulation
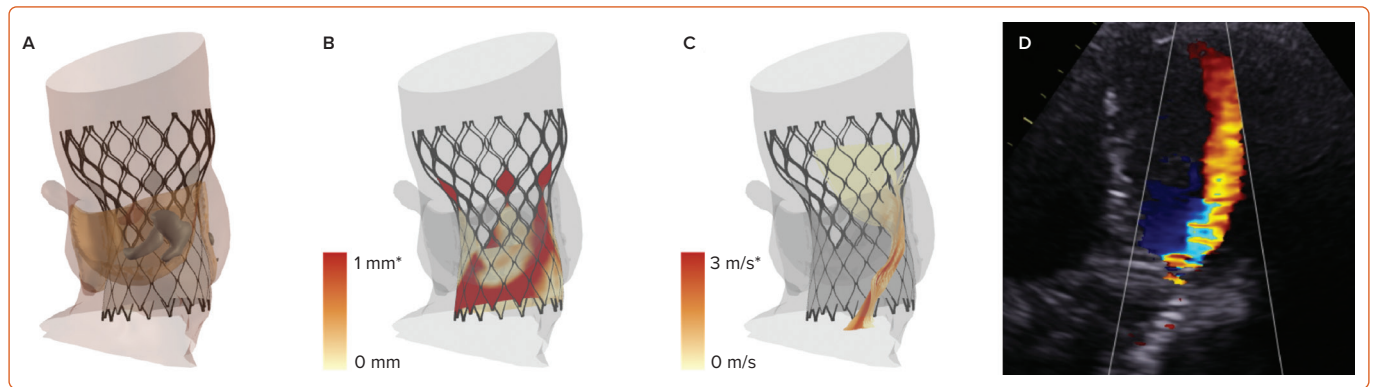
A: Finite element analysis is performed to simulate the interaction between the transcatheter heart valve and the native anatomy. B: Areas of poor apposition are noted. C: The blood domain is extracted and then computational fluid dynamics is used to simulate paravalvular regurgitation. In this example, significant paravalvular regurgitation is predicted. D: Postoperative transthoracic echocardiography demonstrates mild–moderate paravalvular regurgitation. *Values above this maximum are displayed in the highest colour in the scale.

Figure 4: Conduction Disturbance Modelling
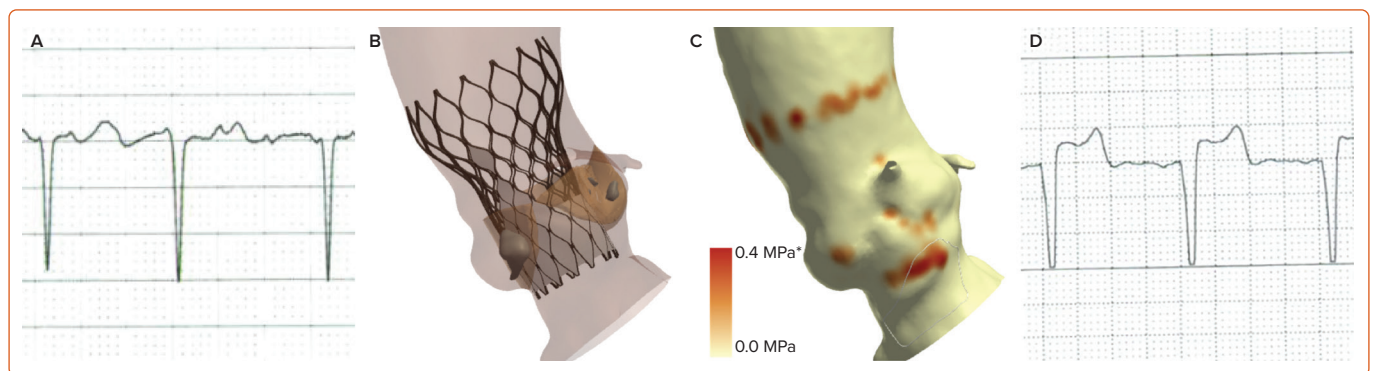
A: A patient with no conduction disturbance underwent transcatheter aortic valve implantation with a 29 mm Evolut R valve. B: Finite element analysis demonstrates elliptical frame deformation within the bicuspid valve. C: Conduction disturbance modelling suggests significant conduction disturbance. D: Following transcatheter aortic valve implantation, the patient developed complete heart block. *Values above this maximum are displayed in the highest colour in the scale.

and conduction disturbance (*Figure 5*).[30] Simulations are performed using a THV sized using the perimeter-derived aortic annulus dimensions, and additional simulations may also be undertaken using a 'downsized' THV. Furthermore, simulations may also be performed with the THV positioned at multiple different implantation depths, typically at a high (0 mm), medium (4 mm), and, in some select cases, a deep (8 mm) implantation depth. Operators may then review the multiple simulations to choose the optimal THV size and implantation depth that reduces predicted paravalvular regurgitation and conduction disturbance.

Prospective Experience

To date, the clinical outcomes of 19 patients who have been treated prospectively using the technology have been presented.[11,25] A significant number of these patients had tricommissural leaflet morphology (47%), but patients with bicommissural raphe-type (37%) and bicommissural non-raphe-type (16%) leaflet morphology were also studied (*Table 1*). The computer simulations have been demonstrated to be a useful aid for guiding treatment decisions in BAV patients. In particular, the CFD analysis may be used to identify patients whose aortic root anatomy may not be suitable for TAVI because of the potential to develop significant paravalvular regurgitation. In prospective clinical usage, the computer simulations have suggested that five patients might develop significant paravalvular regurgitation if treated with a self-expanding THV, and, following discussion in the heart team meeting, four of these patients were treated with surgery. One patient was thought by the heart team to have a too high risk for surgery and was treated with a balloon-expandable THV.

For the 14 patients who were treated with TAVI using a self-expanding THV, the computer simulations were found to be a useful guide for THV sizing and positioning, and in 10 of these patients, procedural aspects were altered to minimise paravalvular regurgitation. In one of these patients, a deep implant was predicted to minimise paravalvular regurgitation and therefore a pre-procedural permanent pacemaker was implanted, given that the computer simulations predicted significant conduction disturbance with a deep implantation depth.

Favourable clinical outcomes have been observed in all 19 patients, with no patient developing moderate paravalvular regurgitation and no patient requiring post-procedural implantation of a permanent pacemaker.

Limitations

It is important that clinicians recognise the limitations of computer modelling. The FEA is not performed in a pressurised state and so is currently unable to simulate important procedural complications such as THV embolisation. Furthermore, the aortic root tissues are modelled with elastic material properties and therefore the FEA is unable to simulate aortic root rupture. The correct modelling of aortic leaflet morphology is dependent on high-quality cardiac CT imaging studies.

Only limited validation of the FEA has been performed for patients with Sievers type 0 (bicommissural non-raphe-type) BAV. The CFD simulations do not have perfect diagnostic accuracy. Conduction disturbance modelling may not be feasible in all patients, given that adequate

Figure 5: Patient-specific Transcatheter Heart Valve Sizing and Positioning
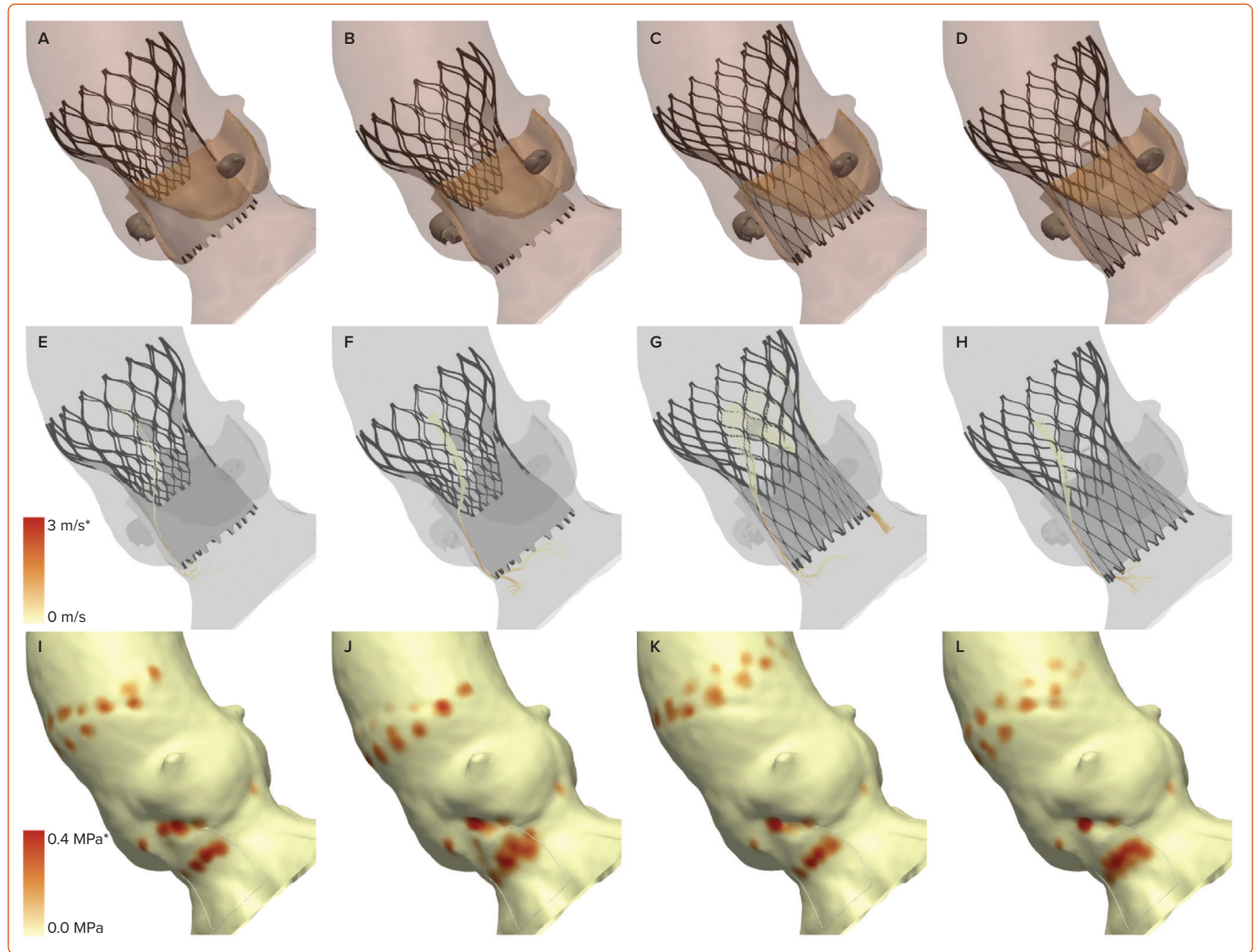
Finite element analysis simulations have been performed with a 29 mm Evolut PRO (A,B) and 34 mm Evolut R (C,D) transcatheter heart valve implanted at high (A,C) and at medium (B,D) implantation depths. The computational fluid dynamics simulations (E–H) and conduction disturbance modelling (I–L) suggest that predicted paravalvular regurgitation and conduction disturbance will be lowest with a 29 mm Evolut PRO transcatheter heart valve positioned at a high implantation depth. *Values above this maximum are displayed in the highest colour in the scale.

Table 1: Baseline Characteristics of Prospectively Treated Patients

Characteristic	n=19
Age (years)	78.9 ± 8.1
Male	13 (68.4)
EuroSCORE II (%)	7.0 ± 6.2
Mean aortic valve gradient (mmHg)	48.6 ± 18.1
Aortic valve morphology	
Sievers classification	
Sievers type 0	3 (15.8)
Sievers type 1	16 (84.2)
TAVR-directed BAVi morphological classification	
Tricommissural	9 (47.4)
Bicommissural raphe type	7 (36.8)
Bicommissural non-raphe type	3 (15.8)

BAVi = bicuspid aortic valve imaging; TAVR = transcatheter aortic valve replacement.

right-sided contrast opacification is required. Although multiple computer simulations may be performed to model a variety of different THV positions, achieving a target implantation depth may not always be feasible with current-generation self-expanding devices, because of the risk of device migration or embolisation on release.[31] Furthermore, repositioning of the THV may induce trauma to the conduction tissue, although this risk might be mitigated by the top-down deployment technique, which is being evaluated in the Optimize PRO study (NCT04091048). The FEops HEARTguide technology is currently unable to model the SAPIEN 3 THV (Edwards Lifesciences), which has been associated with favourable procedural outcomes in bicuspid anatomy, although patient-specific computer simulation of BAV with this THV has been performed by other groups.[22,32] Due to time and financial constraints, use of the technology may not be feasible in all patients, and its usage could potentially be limited to patients with high-risk complex anatomical subsets, such as patients with a calcified raphe or excess leaflet calcification, or for patients with a tapered aortic root anatomy, for whom THV downsizing might be considered.[33,34]

Future Directions

It is important to consider how patient-specific computer simulation of BAV could best be implemented into routine clinical practice. Ideally,

technologies such as deep learning would be used to rapidly identify patients with BAV at the time of cardiac CT acquisition.[35] Cardiac CT imaging might then be transferred onto a cloud-based platform, where deep learning algorithms could assist with automatic segmentation of aortic root structures, reducing case processing times.[36,37] Computer simulation output could then be provided to treating physicians in an expedited manner.[38]

To date, limited prospective experience exists with patient-specific computer simulation of TAVI in BAV. To address this shortcoming, the PRECISE TAVI study (NCT04473443) will examine the role of patient-specific computer simulation in heart team decision-making in complex anatomy.

Optimal THV device selection for bicuspid anatomy is yet to be established and patient-specific computer simulation could potentially be used to guide the selection of a high-radial-force or high-conformity THV.[21]

Ultimately, there exists the potential for patient-specific THVs to be developed, which would be tailored to the patient's precise anatomical characteristics and could potentially reduce both paravalvular regurgitation and conduction disturbance.[26]

Finally, further studies will be needed to determine if hospital outcomes of TAVI in BAV patients might benefit from other uses of artificial intelligence, such as deep learning, which has been demonstrated to be predictive of short-term outcomes in other fields of cardiovascular diseases, such as carotid artery stenting.[39]

Conclusion

As the use of TAVI continues to expand into the younger, lower-risk patient cohort, achieving excellent clinical outcomes in BAV is important. Patient-specific computer simulation is an emerging technology that may be used by the heart team to guide the transcatheter treatment of patients with BAV. ❑

Clinical Perspectives

- Patient-specific computer simulation of transcatheter aortic valve implantation in bicuspid aortic valve may predict the development of important clinical outcomes such as paravalvular regurgitation and conduction disturbance
- Patient-specific computer simulation may be used to optimise transcatheter heart valve sizing and positioning to minimise predicted paravalvular regurgitation and conduction disturbance
- The usage of patient-specific computer simulation to risk-stratify bicuspid patients and to optimise transcatheter heart valve sizing and positioning has been associated with favourable clinical outcomes

1. 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;96:158–66. https://doi.org/10.1002/ccd.28504; PMID: 31566902.
2. 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;111:920–5. https://doi.org/10.1161/01.cir.0000155623.48408.c5; PMID: 15710758.
3. Yoon SH, Bleiziffer S, De Backer O, et al. Outcomes in transcatheter aortic valve replacement for bicuspid versus tricuspid aortic valve stenosis. *J Am Coll Cardiol* 2017;69:2579–89. https://doi.org/10.1016/j.jacc.2017.03.017; PMID: 28330793.
4. Halim SA, Edwards FH, Dai D, et al. Outcomes of transcatheter aortic valve replacement in patients with bicuspid aortic valve disease: a report from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. *Circulation* 2020;141:1071–9. https://doi.org/10.1161/circulationaha.119.040333; PMID: 32098500.
5. Pibarot P, Hahn RT, Weissman NJ, et al. Association of paravalvular regurgitation with 1-year outcomes after transcatheter aortic valve replacement with the SAPIEN 3 valve. *JAMA Cardiol* 2017;2:1208–16. https://doi.org/10.1001/jamacardio.2017.3425; PMID: 28973091.
6. Jørgensen TH, De Backer O, Gerds TA, et al. Mortality and heart failure hospitalization in patients with conduction abnormalities after transcatheter aortic valve replacement. *JACC Cardiovasc Interv* 2019;12:52–61. https://doi.org/10.1016/j.jcin.2018.10.053; PMID: 30621978.
7. El Faquir N, Ren B, Van Mieghem NM, et al. Patient-specific computer modelling: its role in the planning of transcatheter aortic valve implantation. *Neth Heart J* 2017;25:100–5. https://doi.org/10.1007/s12471-016-0923-6; PMID: 27888494.
8. Brouwer J, Nijenhuis VJ, Gheorghe L, et al. The accuracy of patient-specific computer modelling in predicting device size and paravalvular aortic regurgitation in complex transcatheter aortic valve replacement procedures. *Structural Heart* 2020;4:320–8. https://doi.org/10.1080/24748706.2020.1765442.
9. Brouwer J, Gheorghe 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;93:1097–105. https://doi.org/10.1002/ccd.27990; PMID: 30461187.
10. 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;13:1803–12. https://doi.org/10.1016/j.jcin.2020.04.018; PMID: 32682679.
11. 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;13:184–92. https://doi.org/10.1016/j.jcin.2019.07.032; PMID: 31629752.
12. 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. https://doi.org/10.1161/circimaging.119.009178; PMID: 31594409.
13. 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:e005344. https://doi.org/10.1161/circinterventions.117.005344; PMID: 29386188.
14. 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;9:508–12. https://doi.org/10.1016/j.jcin.2016.01.003; PMID: 26965945.
15. 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;11:1044–52. https://doi.org/10.4244/eijv11i9a212; PMID: 26788707.
16. Collas VM, Rocatello G, El Faquir N, et al. Effect of commissural alignment on paravalvular aortic regurgitation after TAVI. *Journal of Heart Valve Disease* 2018–19;28:1–7.
17. Bavo AM, Wilkins BT, Garot P, et al. Validation of a computational model aiming to optimize preprocedural planning in percutaneous left atrial appendage closure. *J Cardiovasc Comput Tomogr* 2020;14:149–54. https://doi.org/10.1016/j.jcct.2019.08.010; PMID: 31445885.
18. de Jaegere P, Rajani R, Prendergast B, et al. Patient-specific computer modeling for the planning of transcatheter mitral valve replacement. *J Am Coll Cardiol* 2018;72:956–8. https://doi.org/10.1016/j.jacc.2018.05.064; PMID: 30115237.
19. Allen CJ, Patterson T, Prendergast B, et al. Simultaneous transcatheter double valve treatment of mediastinal radiation-induced severe calcific aortic and mitral stenosis. *JACC Case Rep* 2020;2:1443–7. https://doi.org/10.1016/j.jaccas.2020.07.003.
20. Karády J, Ntalas I, Prendergast B, et al. Transcatheter mitral valve replacement in mitral annulus calcification: "the art of computer simulation". *J Cardiovasc Comput Tomogr* 2018;12:153–7. https://doi.org/10.1016/j.jcct.2017.12.007; PMID: 29325812.
21. Finotello A, Romarowski RM, Gorla R, et al. Performance of high conformability vs. high radial force devices in the virtual treatment of TAVI patients with bicuspid aortic valve. *Med Eng Phys* 2021;89:42–50. https://doi.org/10.1016/j.medengphy.2021.02.004; PMID: 33608124.
22. Pasta S, Cannata S, Gentile G, et al. Simulation study of transcatheter heart valve implantation in patients with stenotic bicuspid aortic valve. *Med Biol Eng Comput* 2020;58:815–29. https://doi.org/10.1007/s11517-020-02138-4; PMID: 32026185.
23. Lavon K, Marom G, Bianchi M, et al. Biomechanical modeling of transcatheter aortic valve replacement in a stenotic bicuspid aortic valve: deployments and paravalvular leakage. *Med Biol Eng Comput* 2019;57:2129–43. https://doi.org/10.1007/s11517-019-02012-y; PMID: 31372826.
24. Gorla R, Casenghi M, Finotello A, et al. Outcome of transcatheter aortic valve replacement in bicuspid aortic valve stenosis with new-generation devices. *Interact Cardiovasc Thorac Surg* 2021;32:20–8. https://doi.org/10.1093/icvts/ivaa231; PMID: 33201993.
25. Dowling C, Gooley R, McCormick L, et al. TCT CONNECT-121 Ongoing experience with patient-specific computer simulation of transcatheter aortic valve replacement in bicuspid aortic valve. *J Am Coll Cardiol* 2020;76(17 Suppl):B53. https://doi.org/doi:10.1016/j.jacc.2020.09.135.
26. Rocatello G, De Santis G, De Bock S, et al. Optimization of a transcatheter heart valve frame using patient-specific computer simulation. *Cardiovasc Eng Technol* 2019;10:456–68. https://doi.org/10.1007/s13239-019-00420-7; PMID: 31197702.
27. Sievers HH, Schmidtke C. A classification system for the bicuspid aortic valve from 304 surgical specimens. *J Thorac Cardiovasc Surg* 2007;133:1226–33. https://doi.org/10.1016/j.jtcvs.2007.01.039; PMID: 17467434.
28. Jilaihawi H, Chen M, Webb J, et al. A bicuspid aortic valve imaging classification for the TAVR era. *JACC Cardiovasc Imaging* 2016;9:1145–58. https://doi.org/10.1016/j.jcmg.2015.12.022; PMID: 27372022.
29. Kawashima T, Sasaki H. A macroscopic anatomical investigation of atrioventricular bundle locational variation relative to the membranous part of the ventricular septum in elderly human hearts. *Surg Radiol Anat* 2005;27:206–13. https://doi.org/10.1007/s00276-004-0302-7; PMID: 15723154.
30. Dowling C, Bavo A, Mortier P, et al. TCT-414 Patient-specific computer simulation to optimise transcatheter heart valve sizing and positioning in bicuspid aortic valve morphology. *J Am Coll Cardiol* 2018;72(13 Suppl):B167. https://doi.org/

doi:10.1016/j.jacc.2018.08.1576.

31. Kim WK, Schäfer U, Tchetche 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;40:3156–65. https://doi.org/10.1093/eurheartj/ehz429; PMID: 31230081.

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;321:2193–202. https://doi.org/10.1001/jama.2019.7108; PMID: 31184741.

33. Yoon SH, Kim WK, Dhoble A, et al. Bicuspid aortic valve morphology and outcomes after transcatheter aortic valve replacement. *J Am Coll Cardiol* 2020;76:1018–30.

https://doi.org/10.1016/j.jacc.2020.07.005; PMID: 32854836.

34. 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:e007107. https://doi.org/10.1161/circinterventions.118.007107; PMID: 30626202.

35. Dowling C, Astudillo P, Brecker S, et al. Classification of aortic valve morphology using a three-dimensional convolutional neural network. Presented at: PCR London Valves 2019, 17–19 November 2019, London, UK.

36. Astudillo P, Mortier P, Bosmans J, et al. Enabling automated device size selection for transcatheter aortic valve implantation. *J Interv Cardiol* 2019;2019:3591314. https://doi.org/10.1155/2019/3591314; PMID: 31777469.

37. Astudillo P, Mortier P, Bosmans J, et al. Automatic detection

of the aortic annular plane and coronary ostia from multidetector computed tomography. *J Interv Cardiol* 2020;2020:9843275. https://doi.org/10.1155/2020/9843275; PMID: 32549802.

38. Ribeiro JM, Astudillo P, de Backer O, et al. Artificial intelligence and transcatheter interventions for structural heart disease: a glance at the (near) future. *Trends Cardiovasc Med* 2021. https://doi.org/10.1016/j.tcm.2021.02.002; PMID: 33581255; epub ahead of press.

39. Amritphale A, Chatterjee R, Chatterjee S, et al. Predictors of 30-day unplanned readmission after carotid artery stenting using artificial intelligence. *Adv Ther* 2021;38:2954–72. https://doi.org/10.1007/s12325-021-01709-7; PMID: 33834355.