An in vitro evaluation of turbulence after transcatheter aortic valve implantation

Hoda Hatoum, MS,^a Atieh Yousefi, BS,^a Scott Lilly, MD, PhD,^b Pablo Maureira, MD, PhD,^c Juan Crestanello, MD,^b and Lakshmi P. Dasi, PhD^{a,b}

ABSTRACT

Background: This study aimed at assessment of post-transcatheter aortic valve (TAV) replacement hemodynamics and turbulence when a same-size SAPIEN 3 (Edwards Lifesciences Corp, Irvine, Calif) and Medtronic Evolut (Minneapolis, Minn) were implanted in a rigid aortic root with physiological dimensions and in a representative root with calcific leaflets obtained from patient computed tomography scans.

Methods: TAV hemodynamics were studied by placing a SAPIEN 3 26-mm and an Evolut 26-mm in rigid aortic roots and representative root with calcific leaflets under physiological conditions. Hemodynamics were assessed using high-fidelity particle image velocimetry and high-speed imaging. Transvalvular pressure gradients (PGs), pinwheeling indices, and Reynolds shear stress (RSS) were calculated.

Results: (1) PGs obtained with the Evolut and the SAPIEN 3 were comparable among the different models (10.5 ± 0.15 mm Hg vs 7.76 ± 0.083 mm Hg in the rigid model along with 13.9 ± 0.19 mm Hg vs 5.0 ± 0.09 mm Hg in representative root with calcific leaflets obtained from patient computed tomography scans respectively); (2) more pinwheeling was found in the SAPIEN 3 than the Evolut (0.231 ± 0.057 vs 0.201 ± 0.05 in the representative root with calcific leaflets and 0.366 ± 0.067 vs 0.122 ± 0.045 in the rigid model); (3) higher rates of RSS were found in the Evolut (161.27 ± 3.45 vs 122.84 ± 1.76 Pa in representative root with calcific leaflets and 337.22 ± 7.05 vs 157.91 ± 1.80 Pa in rigid models). More lateral fluctuations were found in representative root with calcific leaflets.

Conclusions: (1) Comparable PGs were found among the TAVs in different models; (2) pinwheeling indices were found to be different between both TAVs; (3) turbulence patterns among both TAVs translated according to RSS were different. Rigid aortic models yield more conservative estimates of turbulence; (4) both TAVs exhibit peak maximal RSS that exceeds platelet activation 100 Pa threshold limit. (J Thorac Cardiovasc Surg 2018;156:1837-48)

Principal Reynolds shear stresses at different phases in the cardiac cycle.

Central Message

Assessing hemodynamics and turbulence engendered after TAV replacement with different TAVs is important because it seeks to relate to platelet activation and thus thrombosis.

Perspective

TAVR is a less invasive technique to address aortic stenosis. Current shortcomings of TAVR include reduced leaflet mobility and limited long-term durability. In vitro hemodynamic assessment of TAVs indicated reduced Reynolds shear stress levels, significantly correlated to hemolysis. This observation is in agreement with recent clinical findings with TAVs.

See Editorial Commentary page 1849.

From the Departments of ^aBiomedical Engineering and ^bSurgery, The Ohio State University, Columbus, Ohio; and ^cDepartment of Cardiovascular Surgery, CHU de Nancy, Nancy, France.

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Address for reprints: Lakshmi P. Dasi, PhD, Department of Biomedical Engineering, The Ohio State University, 473 W 12th Ave, Columbus, OH 43210 (E-mail: lakshmi.dasi@osumc.edu).

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Transcatheter aortic valve (TAV) replacement (TAVR) emerged as a percutaneous alternative procedure for surgical aortic valve replacement procedures especially for high-risk patients.^{1,2} To date, all known heart valve prostheses have been associated with clinical complications and adverse effects resulting from

Scanning this QR code will take you to a supplemental video for the article.

Abbreviations and Acronyms

CT	= computed tomography
EOA	= effective orifice area
PG	= pressure gradient
PI	= pinwheeling index
PIV	= particle image velocimetry
RSS	= Reynolds shear stress
TAV	= transcatheter aortic valve
TAVR	= transcatheter aortic valve replacement
TKE	= turbulent kinetic energy

the nonphysiological flow patterns caused by their implantation.^{3,4} Elevated postprocedural pressure gradients (PGs), paravalvular leakage, TAV thrombosis, and many other degenerative effects particularly on the leaflets are some of these adverse outcomes.⁵ The relatively rapid degeneration of TAVs compromise their durability because of the mechanical forces exerted on the leaflets as they interact with the pulsatile blood flow and lead to having the patient go through another probable implantation.^{3,4,6}

TAVs commonly used can be categorized into 2 distinct types: balloon-expandable, and self-expandable. Clinical studies have shown several significant differences between the 2 types, including significantly lower frequency of reduced leaflet motion with self-expandable TAVs such as CoreValve or Evolut (both from Medtronic, Minneapolis, Minn; 4%-6%) compared with 16% for balloon-expandable SAPIEN 3 (Edwards Lifesciences Corp, Irvine, Calif)⁷ while showing a significantly higher rate of moderate to severe paravalvular leakage, significantly greater need for permanent pacemaker implantation, and significantly lower radial force exerted by self-expandable TAVs.^{4,8-13} The distinct physical differences such as leaflet thickness, leaflet shape, stent frame curvature, and stent profile alters TAV hemodynamics and imposes limitations for both devices.¹⁴

Turbulence distal to heart valves during forward flow is the fundamental fluid dynamics phenomenon responsible for PG as well as hemolysis and platelet activation. It is a phenomenon fundamental to any fluid for which there is shearing (velocity changing significantly lateral to the direction of flow). Specifically turbulence occurs when the velocity is high enough that viscosity is unable to diffuse and damp any local fluctuations in velocity leading to an exponential rise of spatial and temporal fluctuations in velocity. These turbulent fluctuations in velocity lead to significantly strong shear stresses that blood cells and platelets experience compared with laminar flows¹⁵⁻¹⁷ and is dependent on the valve geometry (smoothness of inflow, stent elements, etc), leaflet performance (such as flutter), and distal diameter of the aorta relative to the valve orifice area. These turbulent stresses are referred to as Reynolds stresses and have been well

known to correlate with hemolysis and platelet activation. Nonphysiological turbulent flow after valve implantation was associated with blood damage ranging from platelet activation (to probably thrombosis) and hemolysis.¹⁸⁻²² Several in vitro studies investigated the risk of platelet activation post-TAVR and set some thresholds that mark the onset of platelet activation from 10 to 100 Pa.^{3,6,23-30} Some of these in vitro studies include Hung and colleagues, who reported platelet damage at 100 to 165 dynes/cm² with an exposure time of 102 seconds.³¹ Williams reported the onset of platelet activation at 130 dynes/cm² under an exposure time of 1023 seconds.³² Ramstack and colleagues reported that platelets are activated at 300 to 1000 dynes/cm² at an exposure time of 10 seconds.³³ With all these data and keeping in mind the basic differences between the SAPIEN and the Evolut TAVs, it is thus crucial to assess the turbulence engendered after TAVR with these 2 distinct TAV types.

In this study, the turbulence engendered immediately downstream of a TAVR valve is evaluated when a SAPIEN and when a Medtronic Evolut are implanted in a rigid aortic root with physiological dimensions and in a calcified representative root with calcific leaflets obtained from patient computed tomography (CT) scans. The purpose of the latter is to assess the effect of more realistic deployment conditions for the 2 TAVs on the turbulence of the forward flow distal to the valves. To our knowledge no comparative study of in vitro leaflet kinematic assessment and Reynolds shear stress (RSS) characterization have been performed across different TAVs. Such a comparison is essential to improve future TAV designs and might provide a rationale behind adverse clinical outcomes.³⁴⁻³⁷

METHODS

Valve Selection and Deployment

To evaluate post-TAVR hemodynamics and turbulence using self-expanding and balloon-expandable TAVs, measurements described herein were conducted with a 26-mm Medtronic Evolut and a 26-mm Edwards SAPIEN 3 implanted in rigid aortic roots and representative root with calcific leaflets obtained from patient CT scans shown in Figure 1. The ascending diameter of the aorta in the rigid model was 31.75 mm, which allows for the Evolut—with an upper part diameter of 32 mm—not to be compressed. The selection of the appropriate aortic root models matched each of the TAV sizes and was on the basis of the recommendations of Kasel and colleagues.³⁸ Distensible extensions were added to the roots to connect to our experimental flow loop setup. Leaflet calcification is shown in Figure 1, C, and is used to assess the effect of calcification on the hemodynamic performance of the TAVs. Hatoum and colleagues³⁹ have detailed the patient-specific design.

Hemodynamic Assessment

Hemodynamic parameters were evaluated under pulsatile flow conditions created by a left heart simulator yielding physiological flow and pressure curves as previously described.^{40,41} The working fluid in this study was a blood analogue mixture of water and glycerine (99% pure glycerine) producing a density of 1060 kg/m³ and a kinematic viscosity of $3.5 \cdot 10^{-6}$ m²/s. Sixty consecutive cardiac cycles of aortic

FIGURE 1. A, Rigid aortic valve chamber with sinuses. B, Patient-specific aortic root models with end extensions. C, Aortic side view of the 3-D printed leaflet calcifications in the patient-specific models. *NCC*, Noncoronary cusp; *LCC*, left coronary cusp; *RCC*, right coronary cusp.

pressure, ventricular pressure, and flow rate data were recorded at a sampling rate of 100 Hz. The mean transvalvular PG is defined as the average of positive pressure difference between the ventricular and aortic pressure curves during forward flow.

The effective orifice area (EOA) is an important parameter to evaluate valve orifice opening. EOA was computed using the Gorlin's equation:

$$EOA = \frac{Q}{51.6\sqrt{PG}}$$

where Q represents the root mean square aortic valve flow over the same averaging interval of the PG.

The pinwheeling index (PI) is an indication with implications on leaflet durability and resilience.⁴²⁻⁴⁴ It is computed from still frames obtained from high-speed imaging as follows and in accordance with Midha and colleagues⁴⁵:

$$PI = \frac{L_{actual} - L_{ideal}}{L_{ideal}}$$

where L_{actual} represents the deflected free edge of the leaflet and L_{ideal} represents the unconstrained ideal configuration of the leaflet free edge.

Particle Image Velocimetry

For particle image velocimetry (PIV), the flow was seeded with fluorescent PMMA-Rhodamine B particles with diameters ranging from 1 to 20 μm . For all cases, the velocity fields within the distal flow region were measured using high spatial and temporal resolution PIV. Briefly, this involved illuminating the flow region using a laser sheet created by pulsed neodymium-doped yttrium lithium fluoride single-cavity diode pumped solid state laser coupled with external spherical and cylindrical

lenses while acquiring high-speed images of the fluorescent particles within the region. Time-resolved PIV images were acquired with resulting spatial and temporal resolutions of 0.0723 mm per pixel and 1000 Hz, respectively. Phase locked measurements were recorded for 4 phases of the cardiac cycle (acceleration, peak, deceleration, and diastole) repetitively 250 times with a spatial resolution of 0.0723 mm per pixel. Refraction was corrected using a calibration in DaVis PIV software (DaVis 7.2; Lavisision, Göttingen, Germany). Velocity vectors were calculated using adaptive cross-correlation algorithms. Further details of PIV measurements can be found elsewhere.^{4,46}

Vorticity Dynamics

Using the velocity measurements from PIV, vorticity dynamics were also evaluated distal to the valve. Vorticity is the curl of the velocity field and therefore captures rotational components of the blood flow shearing as well as visualizing turbulent eddies. Regions of high vorticity along the axis perpendicular to the plane indicate shear and rotation of the fluid particles. Vorticity was computed using the following equation:

$$\omega_z = -\left(\frac{dV_x}{dy} - \frac{dV_y}{dx}\right)$$

where ω_z is the vorticity component with units of s^{-1} ; V_x and V_y are the x and y components of the velocity vector with units of m/s. The x and y directions are axial and lateral, respectively, with the z direction being out of measurement plane.

RSS and Turbulent Kinetic Energy

RSS has been widely correlated to turbulence and platelet activation.^{18,19} It is a statistical quantity that measures the shear stress

TABLE 1. Average hemodynamic parameters of the different valves

Valve type	Model type	ΔP , mm Hg	EOA, cm^2	RF, %	Pinwheeling index	Peak RSS, Pa
Evolut (Medtronic, Minneapolis, Minn)	Patient-specific	13.9 ± 0.19	1.5 ± 0.004	32.10 ± 0.70	0.201 ± 0.05	161.27 ± 3.45
	Rigid	10.5 ± 0.15	1.8 ± 0.036	15.74 ± 0.73	0.122 ± 0.045	337.22 ± 7.05
SAPIEN 3 (Edwards Lifesciences Corp, Irvine, Calif)	Patient-specific	5.0 ± 0.09	1.7 ± 0.011	23.75 ± 0.75	0.231 ± 0.057	122.84 ± 1.76
	Rigid	7.76 ± 0.083	2.1 ± 0.025	10.92 ± 0.11	0.366 ± 0.067	157.91 ± 1.80

Values reported are $\pm$ SD. ΔP , Transvalvular pressure gradient (mm Hg); EOA, effective orifice area; RF, regurgitant fractions (%); RSS, Reynolds shear stress.

	Acceleration	Peak	Deceleration	Diastole
Patient-specific Model with Evolut 26
Patient-specific Model with SAPIEN 26
Rigid Model with Evolut 26
Rigid Model with SAPIEN 26

FIGURE 2. En face imaging of the valves at different phases in the cardiac cycle. The Evolut valve is from Medtronic (Minneapolis, Minn) and the SAPIEN valve is from Edwards Lifesciences Corp (Irvine, Calif).

between fluid layers when fluid particles decelerate or accelerate while changing direction.²⁶ Turbulent kinetic energy (TKE) is a measurement of the kinetic energy of eddies and indicates turbulence intensity²⁶:

$$RSS = \rho \sqrt{\left(\frac{u'u' - v'v'}{2} \right)^2 + (u'v')^2}$$

where ρ is the blood density and u' and v' are the instantaneous velocity fluctuations in the x and y directions, respectively.

$$TKE = \frac{1}{2} \left(\overline{u'^2 + v'^2} \right)$$

Statistics

Statistical analysis in this study was performed using JMP Pro version 13.0.0 (SAS Institute Inc, Cary, NC). All data are presented as mean $\pm$ standard error. Student *t* test was used to compare the means and $P < .05$ was considered statistically significant. Analyses were performed over 60 replicates.

RESULTS

Hemodynamic Parameters

Table 1 shows hemodynamic parameters obtained from flow and pressure data for the different valves in the

different models. In the rigid model, the Evolut yielded higher PG (10.5 ± 0.15 mm Hg) thus lower EOA (1.8 ± 0.036 cm²) compared with the SAPIEN 3

VIDEO 1. En-face imaging views of the valves throughout the cardiac cycle. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)31464-8/fulltext](https://www.jtcvs.org/article/S0022-5223(18)31464-8/fulltext).

FIGURE 3. Phase averaged velocity vectors and vorticity contours at different phases in the cardiac cycle. The Evolut valve is from Medtronic (Minneapolis, Minn) and the SAPIEN valve is from Edwards Lifesciences Corp (Irvine, Calif).

(7.76 ± 0.083 mm Hg and 2.1 ± 0.025 cm², respectively; $P < .001$). In the representative root with calcific leaflets model, similarly, the Evolut yielded higher PG (13.9 ± 0.19 mm Hg) thus lower EOA (1.5 ± 0.004 cm²) compared with the SAPIEN 3 (5.0 ± 0.009 mm Hg and 1.7 ± 0.011 cm², respectively; $P < .001$).

The Evolut and the SAPIEN 3 yielded different PGs in the representative root with calcific leaflets models compared with the rigid ones (13.9 ± 0.19 mm Hg vs 10.5 ± 0.15 mm Hg for the Evolut and 5.0 ± 0.09 mm Hg vs 7.76 ± 0.083 mm Hg for the SAPIEN; $P < .001$).

Leaflet Kinematics and PI

Figure 2 shows en-face images of every valve in each of the representative root with calcific leaflets and rigid models at 4 phases of the cardiac cycle on the basis of flow: acceleration, peak, deceleration, and diastole. Video 1 shows the valve leaflets deformations and the significant central coaptation region twisting or pinwheeling. In the representative root with calcific leaflets model, the onset of the opening and the closure starts with 1

leaflet (bottom right leaflet) followed by the 2 others with the Evolut. However for the SAPIEN 3, the opening and closing mechanism is symmetrical. Both valves nevertheless fully open at peak systole. In the rigid model, the Evolut and the SAPIEN 3 open and close fully and symmetrically with all 3 leaflets together. In both models, the Evolut leaflets show more flutter compared with the SAPIEN 3.

The pinwheeling indices are shown in Table 1. The SAPIEN 3 showed higher pinwheeling indices in the representative root with calcific leaflets and rigid models compared with the Evolut (0.231 ± 0.057 vs 0.201 ± 0.05 in the representative root with calcific leaflets model and 0.366 ± 0.067 vs 0.122 ± 0.045 in the rigid model). The coaptation mismatch in the SAPIEN 3 led to warping of the leaflets' edges. The Evolut yielded higher PI in the representative root with calcific leaflets model than in the rigid one (0.201 ± 0.05 vs 0.122 ± 0.045 in the representative root with calcific leaflets model vs rigid one). However the differences were not significant ($P = .12$). The SAPIEN 3, however, showed the opposite

VIDEO 2. Ensemble averaged velocity vectors and vorticity contours for the valves. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)31464-8/fulltext](https://www.jtcvs.org/article/S0022-5223(18)31464-8/fulltext).

(0.231 ± 0.057 vs 0.366 ± 0.067 in the representative root with calcific leaflets model vs rigid one), although the differences were not significant ($P = .06$).

Flow Velocity Field

Flow velocity field is an important indicator of the velocity and vorticity state of the flow highlighting high-velocity and high-rotation regions. The flow velocity field clearly shows the differences after implantation of many different TAVs. Because velocity is an important factor in evaluating post-TAVR dynamics clinically, velocity fields provide this comprehensive information. **Figure 3** shows the phase averaged velocity vectors and vorticity contours at the 4 different phases in the cardiac cycle for the different valves and models. **Video 2** shows an animation of the flow field development (vorticity contours and velocity vectors) throughout 1 cardiac cycle for each model and valve, and **Video 3** shows the fluid particle streaks for every valve case in every model over the cardiac cycle. The dark streaks of red and blue vorticity contours represent the shear layers corresponding to the jet boundaries and the distance between them represents the width of the jet. Shear layers appear during the acceleration phase.

In a comparison of the representative root with calcific leaflets models, the velocity with the Evolut starts at 0.88 m/s during acceleration to reach 2.3 m/s at peak systole, then 1.3 m/s during deceleration. With the SAPIEN 3, the velocity starts at 0.46 m/s during acceleration, reaches 1.65 m/s at peak systole, then 0.62 m/s during deceleration. The velocity is near 0 during diastole for both cases reaching a maximum of 0.2 m/s. It is clear that in the representative root with calcific leaflets models, the shear layers at peak systole diffuse laterally along the flow direction with more diffusion distal to the Evolut.

VIDEO 3. Main flow streak visualization of the different valves. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)31464-8/fulltext](https://www.jtcvs.org/article/S0022-5223(18)31464-8/fulltext).

In a comparison of the rigid models, the velocity with the Evolut starts at 1.00 m/s during acceleration to reach 2.45 m/s at peak systole, then 1.37 m/s during deceleration. With the SAPIEN 3, the velocity starts at 0.86 m/s during acceleration, reaches 2.10 m/s at peak systole, then 0.94 m/s during deceleration. The velocity is near 0 during diastole reaching a maximum of 0.19 m/s for both cases.

Compared with the representative root with calcific leaflets models, the shear layers and vortical structures in the rigid models with both valves exhibit a more stable and steady behavior especially during peak systole. Lateral turbulent diffusion, however, is more prevalent in the Evolut in accordance with the results observed in the representative root with calcific leaflets models. The peak vorticity was calculated to be 565 seconds^{-1} for the Evolut in the representative root with calcific leaflets model, 668 seconds^{-1} for the SAPIEN with representative root with calcific leaflets model, 676 seconds^{-1} for the Evolut with the rigid model and 851 seconds^{-1} for the SAPIEN with the rigid model. Parallelism of the shear layers (tendency of the shear layers to remain parallel to each other) is more maintained in the rigid models, particularly with the SAPIEN.

RSS Fields

The importance of RSS arises from its connection to platelet activation and its account of the turbulent fluctuations of the blood velocity.¹⁸⁻²² **Figure 4** shows the principal RSSs at different phases in the cardiac cycle for the different valves and models. The contour plots of the RSS mirror those of the vortical shear layer structures in **Figure 3** with RSS peaking in areas with more diffused shear layer vorticity.

The Evolut and the SAPIEN 3 valves exhibit higher RSS in the acceleration phase with the rigid model than the representative root with calcific leaflets model. Peak RSS in that phase reaches 46.05 Pa for the rigid model with Evolut and 59.9 Pa for the rigid model with SAPIEN. The

FIGURE 4. Principal Reynolds shear stress (RSS) at different phases in the cardiac cycle. The Evolut valve is from Medtronic (Minneapolis, Minn) and the SAPIEN valve is from Edwards Lifesciences Corp (Irvine, Calif).

RSS was calculated to be 9.40 and 8.87 Pa in the representative root with calcific leaflets model for Evolut and SAPIEN respectively.

During peak systole, the Evolut shows higher RSS distributions and magnitudes compared with the SAPIEN in representative root with calcific leaflets and rigid models. Table 1 shows the peak RSS values. In the representative root with calcific leaflets models, RSS were equal to 161.27 Pa and 122.84 Pa with the Evolut and SAPIEN, respectively. In the rigid model, RSS were equal to 337.22 Pa and 157.91 Pa with the Evolut and SAPIEN, respectively. It is also clear that the rigid models show higher RSS magnitudes with both valves.

After the peak, RSS decreases throughout deceleration and diastole. During deceleration, the maximum RSS obtained was with the Evolut in the rigid model (164.5 Pa).

TKE

TKE is the energy in velocity fluctuations and is dissipated by viscous forces through intense temporal events of blood shearing. It indicates how turbulent the

blood flow is, thus giving an idea about the performance of the TAV implanted. TKE contour plots in Figure 5 mirror those of the RSS. Thus, the Evolut exhibits the highest TKE levels compared with the SAPIEN in both models particularly at peak systole. In the representative root with calcific leaflets model with Evolut, peak TKE was calculated to be $0.39 \text{ m}^2/\text{s}^2$ whereas the SAPIEN in the same model exhibited a TKE of $0.29 \text{ m}^2/\text{s}^2$. In the rigid model with Evolut, TKE was calculated to be $0.59 \text{ m}^2/\text{s}^2$ whereas the SAPIEN gave a value of $0.30 \text{ m}^2/\text{s}^2$.

Turbulent Velocity Fluctuations

Velocity fluctuations are characteristics of turbulent flow. These fluctuations give an indication about how turbulent the blood flow is thus providing an assessment of the TAV performance. Figure 6 shows the standard deviation contour plots of the turbulent velocity fluctuations U' and V' for the different valves and models at peak systole. As is the case for RSS and TKE, a large U' root mean square (RMS) or V'_{RMS} indicate a higher level of turbulence. U'_{RMS} and V'_{RMS} are highest with the Evolut in representative root with

FIGURE 5. Turbulent kinetic energy (TKE) at different phases in the cardiac cycle. The Evolut valve is from Medtronic (Minneapolis, Minn) and the SAPIEN valve is from Edwards Lifesciences Corp (Irvine, Calif).

calcific leaflets and rigid models (0.55 m/s and 0.44 m/s vs 0.76 m/s and 0.51 m/s, respectively).

To better assess the turbulent velocity fluctuations, the instantaneous velocity taken at 2 different points (labeled A and B) on the respective shear layers of the 4 valve cases are plotted versus the cardiac cycle time in the x and y directions. The plots are shown in Figure 7 and a summary of the values is given in Table 2. Time fluctuations are assessed in terms of the SDs of these plots and are associated with the degree of turbulence. The plots show clearly that at point A, the rigid model with the Evolut valve shows more spread out fluctuations in the x direction (SD 0.58 m/s) and the representative root with calcific leaflets model with the Evolut shows more fluctuations in the y direction (SD 0.194 m/s). At point B, the representative root with calcific leaflets model with Evolut shows higher fluctuations in the x and y directions (0.752 m/s and 0.211 m/s, respectively). The fluctuations in the y direction are higher in the representative root with calcific leaflets models with both valves compared with those of the rigid models at points A and B.

DISCUSSION

In this study, the differences engendered as a result of the 2 different TAVs (Evolut and SAPIEN) was assessed via: (1) hemodynamic parameters; and (2) turbulence in 2 different models, one rigid and another representative root with calcific leaflets. The importance of studying turbulence post-TAVR stems from its effect on platelet activation, hemolysis, and effects on pressure drop and recovery. Also, the importance of studying the idealized versus realistic aortic root is to assess how baseline design of these valves does not necessarily translate to the in situ setting.

Effect of Anatomically Realistic Valve Mounting on Hemodynamic Parameters

The different TAVs yielded different hemodynamic parameters specifically in terms of PGs. The most striking differences were seen between the representative root with calcific leaflets models and the rigid models with the main difference being that in the rigid model the valves were deployed in an idealistic manner and reached their full potential in an idealized circular orifice. However, in

FIGURE 6. Standard deviation contour plots of the random velocity fluctuations U' and V' for the different valve models at peak systole. The Evolut valve is from Medtronic (Minneapolis, Minn) and the SAPIEN valve is from Edwards Lifesciences Corp (Irvine, Calif). *RMS*, Root mean square.

the representative root with calcific leaflets models the valves were deployed in an anatomically realistic configuration. The noncircular anatomy and calcification on and around the leaflets in the representative root with calcific leaflets models clearly play an important role in the apposition of the TAV, and thus its sealing.^{4,47,48} The leaflet stiffness in this model also plays a role in the valve shape post-deployment because a noncircular final shape might be a consequence, in addition to the distribution of the calcium adding to this stiffness and helping the noncircular and noncomplete apposition of the TAV. Because the SAPIEN is balloon-expandable, PGs were lower because the radial force exerted by the balloon gives the SAPIEN 3 an advantage in this case.^{4,47,48}

Leaflet Kinematics and PI

PI is a dimensionless index used to quantify valve leaflet deformation severity and coaptation mismatch. High PIs are often associated with low durability, and therefore accelerated failure of valve leaflets.⁴²⁻⁴⁴ The SAPIEN showed higher pinwheeling indices than the Evolut in the representative root with calcific leaflets and rigid models. This might be because of the higher compression near the region of the leaflets in the SAPIEN compared with the

supra-annular design of the Evolut in which stresses are not as much.⁴⁴ Chakravarty and colleagues⁷ have shown in vivo data with more leaflet thrombosis prevalent in the SAPIEN than Evolut. In [Video 1](#), it is clear that during peak flow, the SAPIEN 3 leaflets almost touch the stent inhibiting flow in the neosinus⁴⁹ contrary to the Evolut, for which the supra-annular leaflet position along with the curved stent design allow for washout. It should be noted that pinwheeling is root and native valve calcium-induced geometry specific. The values shown in this study cannot be generalized and actual pinwheeling will be very patient-dependent. However, it is interesting that the SAPIEN valve pinwheeled more despite its advantage in orifice opening underpinning some fundamental design influences in how the leaflets are shaped and mounted in the 2 valves. Further studies are clearly needed to assess which valve is more “robust” to avoid pinwheeling. Pinwheeling is also dependent on the maximum expansion allowed and the extent of eccentricity of the orifice.

Flow Velocity Field and Vorticity Dynamics

The flow velocity fields and shear layers are different among the different valves and the models. The better apposition of the SAPIEN in the calcified aortic root as

FIGURE 7. A and C, Instantaneous velocity in the x direction (U) and (C) and (D) instantaneous velocity in the y direction (V) plots of the different valve combinations through the cardiac cycle at points (A and B), respectively, in the shear layers. The Evolut valve is from Medtronic (Minneapolis, Minn) and the SAPIEN valve is from Edwards Lifesciences Corp (Irvine, Calif).

previously explained provides more flow area thus lower jet velocity compared with the Evolut in the representative root with calcific leaflets models. In the rigid models, the SAPIEN yields lower velocities. This is in concordance with the PG data explained previously.

Turbulence is characterized by high levels of fluctuating vorticity. For this reason, vorticity dynamics play an essential role in the description of turbulent flows.⁵⁰ Turbulent flows always exhibit high levels of fluctuating vorticity as is evident in Figure 3 contours and Video 2. In addition, shear layers in both TAVs seem to dissipate and to exhibit an unsteady behavior more quickly in the representative root with calcific leaflets models compared with the rigid ones. The reason behind that might be attributed to the flexible and more complex boundaries in the representative root with calcific leaflets models. In a

TABLE 2. SDs of the velocities in the x and y directions (U and V , respectively) at points A and B for the different valve combinations during the cardiac cycle

	Patient-specific model		Rigid model	
	Evolut	SAPIEN	Evolut	SAPIEN
SD, m/s				
x direction				
Point A	0.389	0.303	0.580	0.394
Point B	0.752	0.541	0.522	0.750
y direction				
Point A	0.194	0.187	0.149	0.128
Point B	0.211	0.143	0.159	0.136

The Evolut valve is from Medtronic (Minneapolis, Minn) and the SAPIEN valve is from Edwards Lifesciences Corp (Irvine, Calif).

flexible medium, flow waves tend to be stabilized when the boundary has a compliant response to them but it was found that the effect of internal friction in the flexible medium might be destabilizing.^{51,52}

RSS Field

The importance of RSS arises from its connection to platelet activation and its account of the turbulent fluctuations of the blood velocity.¹⁸⁻²² Reynolds stress is produced when fluid particles decelerate or accelerate while changing direction.²²

The SAPIEN yielded lower RSS in representative root with calcific leaflets and rigid models compared with the Evolut, specifically at peak systole. This difference might be attributed to the distal meshed stent frame of the Evolut that protrudes along the sinotubular junction. Turbulence studies have emphasized the effect of porous media on increasing the flow turbulence, unsteadiness, and chaos.^{53,54} In addition, studies have shown that the presence of grids enhances turbulence, promotes rapid decay and diffusion axially, and increases skewness of the velocity fluctuation.⁵⁵ This highlights the effect of the Evolut stent on the higher RSS calculated in the representative root with calcific leaflets and rigid models.

In addition, the representative root with calcific leaflets models provide lower RSS values compared with the rigid ones. The reason is because the compliant walls cause fluctuations thus dissipating RSS.⁵¹

On the basis of the peak RSS values calculated, it seems that both TAVs cross the threshold of 100 Pa, defined as

the onset of platelet activation,^{3,33,56} whether in the representative root with calcific leaflets or the rigid models, with the rigid models yielding more conservative—as in higher—estimates. The SAPIEN's peak values come in accordance with those found in a similar study by Gunning and colleagues.²⁶ One in vitro study highlighted the effect of the SAPIEN structure on enhancing platelet activation and thus thrombus formation.⁵⁷ Ultimately, because all cases exceed 100 Pa, TAV leaflet thrombosis is dependent on many factors besides RSS, mainly sinus washout.^{41,58}

TKE and Velocity Fluctuations Effect

TKE and U'_{RMS} and V'_{RMS} are closely related as was introduced in the Methods. Because the velocity fluctuations in the x direction occur prevalently in both models with SAPIEN and Evolut TAVs, the main element of focus is the fluctuation in the lateral (y) direction. The fluctuations in the y direction are tightly related to the unsteadiness explained previously in the velocity and vorticity fields. Because in the representative root with calcific leaflets models unsteadiness prevails compared with the rigid models, it is intuitive to have high lateral direction fluctuations. Similarly, as discussed previously, the Evolut stent yields more unsteadiness causing the higher fluctuations with the Evolut than the SAPIEN. TKE contours reinforce these results. In addition, the more significant leaflet flutter observed in Video 1 with Evolut in both models comes in agreement with these lateral fluctuations and enhance the generated turbulence.

Limitations

The experiments conducted in this study investigated 2 distinct valves of the same size, 26 mm: a Medtronic Evolut and an Edwards SAPIEN. Although not anticipated, valve-to-valve variability (for the same size) is not addressed in this study. That said, the lack of a curved aorta is an additional limitation. Future studies are needed for capturing the influence of aortic curvature on any modification of turbulence distal to the valve. Another limitation might be related to the precise interaction between the valve stent and the 3-D printed native leaflets because there is large variability between patients in the stiffness of the leaflets. Short axis PIV is also lacking and studies using stereo capabilities or tomographic PIV systems are needed.

CONCLUSIONS

The hemodynamic performance and turbulence of two 26-mm TAVs (Medtronic Evolut and Edwards SAPIEN 3) in rigid and representative root with calcific leaflets obtained from patient CT scans models were assessed and compared in this study. The main hemodynamic parameters in terms of PGs were of the same order whereas pinwheeling indices were higher with the SAPIEN 3. The flow among

both TAVs was different in terms of velocity fields, shear layer characteristics, RSS values, and contours along with velocity fluctuations. Whereas the SAPIEN 3 showed higher rates of pinwheeling, it was accompanied by lower rates of RSS compared with the Evolut because of the Evolut's distal stent structure interacting with the flow. Despite achieving less RSS, the SAPIEN still exhibited RSS that exceeds the threshold for platelet activation, which might explain the higher thrombosis risk found in vivo.

Conflict of Interest Statement

Dr Crestanello reports grants from Medtronic, Boston Scientific, and Abbot during the conduct of the study, and serves on the advisory board of Medtronic. Dr Dasi and Ms Yousefi report having 2 patent applications for The Ohio State University on novel surgical and transcatheter valves. All other authors have nothing to disclose with regard to commercial support.

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