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Transcatheter aortic valve implantation with the Portico and Evolut R bioprostheses in patients with elliptic aortic annulus

Riccardo Gorla[1], MD, PhD; Federico De Marco[1], MD, PhD; Simone Morganti[2], MSc, PhD; Alice Finotello[2], MSc; Nedy Brambilla[1], MD; Luca Testa[1], MD, PhD; Mauro Luca Agnifili[1], MD; Maurizio Tusa[1], MD; Ferdinando Auricchio[3], MSc, PhD; Francesco Bedogni[1]*, MD

1. Department of Clinical and Interventional Cardiology, IRCCS Policlinico San Donato, Milan, Italy; 2. Department of Electrical, Computer, and Biomedical Engineering, University of Pavia, Pavia, Italy; 3. Department of Civil Engineering and Architecture, University of Pavia, Pavia, Italy

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Introduction

Among anatomical factors affecting transcatheter aortic valve implantation (TAVI) success, aortic annulus shape plays a relevant role: an elliptic geometry may lead to gaps between the aortic root and the prosthesis, which is designed to expand circularly, resulting in paravalvular leak (PVL). In this context, the impact of different self-expanding (SE) devices is currently unknown.

The aim of the study was to compare PVL and device success rates of the Portico and Evolut R in patients with an elliptic aortic annulus and to test by computational simulations their behaviour by increasing eccentricity.

Methods

This retrospective study included 374 patients with symptomatic severe aortic stenosis undergoing TAVI with the Portico™ (Abbott Vascular, Santa Clara, CA, USA) and Evolut™ R (Medtronic, Minneapolis, MN, USA) valves and with available computed tomography (CT) angiography measurements of the aortic annulus **(Supplementary Figure 1)**.

The index of eccentricity (IE) was calculated as (1–short-axis/long-axis annulus diameter); IE >0.25 defined an elliptic aortic annulus[1].

Post-procedural PVL was assessed with transthoracic echocardiography and classified into four categories (absent/trivial, mild, moderate, severe) by experienced echocardiographers who were blinded to the aortic annulus measurements[2].

Device success was defined according to the VARC-2 definition[2].

Geometrical models of the Evolut R and Portico were reconstructed from micro-CT scans of real device samples (Evolut R 26 mm and Portico 25 mm) and nitinol material properties were assigned **(Supplementary Figure 2)**; an idealised model of the aortic root was conceived with increasing eccentricities (0/0.25/0.5) and used for finite element simulation of TAVI[3] **(Supplementary Figure 3)**. Post-processing of simulation outcomes was performed to compute stent-root interaction area, von Mises stress distribution of the LVOT/annulus region, and paravalvular orifice area. Statistical methods are detailed in **Supplementary Appendix 1**.

**Corresponding author: Department of Clinical and Interventional Cardiology, IRCCS Policlinico San Donato, Piazza Edmondo Malan, 2, 20097 San Donato Milanese, Milan, Italy. E-mail: Francesco.bedogni@grupposandonato.it*

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Results

Of 374 patients, 107 (28.6%) had an elliptic annulus and were more frequently women **(Table 1)**. Elliptic annulus patients were equally distributed in the Portico and Evolut R groups (25.2% vs 30.0%; p=0.35); among them, oversizing was greater in the Evolut R than in the Portico group, whereas the predilatation rate and implantation depth were overall higher in Portico patients **(Table 2)**. Postoperatively, ≥moderate PVL rate was similar between Portico and Evolut R patients (7.2% vs 8.4%; p=0.71). Higher rates of ≥moderate PVL were observed in the elliptic group only in Evolut R patients **(Table 2)**. Device success was comparable between Portico and Evolut R patients (91.9% vs 90.5%; p=0.67). Causes of device failure were ≥moderate PVL in 30 (88.2%) patients and implantation of a second prosthesis in 4 (11.8%) patients.

Among elliptic annulus patients, device success was higher in the Portico group than in the Evolut R group **(Figure 1A)**. On the other hand, device success in the Evolut R elliptic group was lower compared to that of non-elliptic annulus patients **(Figure 1A)**, mainly driven by a higher rate of ≥moderate PVL in the former (15.2% vs 5.4%; p=0.009).

On receiver operating characteristic (ROC) curve analysis, eccentricity was predictive of device success only among Portico patients **(Figure 1B, Figure 1C)**.

On simulation analysis, the Portico device maintained substantially similar values of stent-root interaction area and symmetric patterns of stress distribution by increasing eccentricity from 0.25 to 0.5, whereas the Evolut R showed a sudden drop, resulting in a steep increase in paravalvular orifice area by IE=0.5 as compared to the Portico **(Figure 1D-Figure 1F, Figure 2)**.

Table 1. Baseline characteristics.

Variables	Overall	Elliptic	Non-elliptic	*p*-value
No. of patients	374	107	267	–
Age (years)	83.6±6.9	83.4±8.4	83.8±6.2	0.69
Female sex	212 (56.7%)	72 (67.3%)	140 (52.4%)	0.009
Coronary artery disease	180 (48.1%)	47 (43.9%)	133 (49.8%)	0.30
STS score (%)	5.9±3.8	6.4±4.0	5.8±3.7	0.21
Ejection fraction (%)	53.1±10.7	53.2±12.7	53.1±9.9	0.950
Mean aortic gradient (mmHg)	44.6±16.6	43.6±16.1	45.1±16.9	0.56
Annulus mean diameter (mm)	23.4±2.4	22.9±2.3	23.7±2.5	0.015
Index of eccentricity	0.22±0.07	0.30±0.04	0.19±0.05	<0.001
Annulus perimeter (mm)	74.2±7.9	73.2±7.2	74.6±8.1	0.15
Annulus area (mm^2)	416.6±116.5	391.5±109.9	424.7±117.8	0.023
Calcium volume 850 HU (mm^3)	220.1 (131.9-404.1)	181.6 (90.2- 422.6)	220.6 (143.7- 401.6)	0.18

Discussion

The issue of aortic annulus eccentricity has been investigated in only a few studies. Maeno et al reported higher rates of device success and lower rates of at least moderate PVL in elliptic annulus patients treated with balloon-expandable (BE) rather than SE devices. This is due to the higher radial force of BE valves which reshape the geometry of the aortic annulus from elliptic to circular, in contrast with the CoreValve® (Medtronic)[4,5]. However, in patients with very elliptic annuli (IE >0.30, 13.9% in our study), BE devices may injure the aortic root, whereas a highly conformable SE device may be safer and equally effective.

Table 2. Procedural outcome.

Variables	Overall	Elliptic			Non-elliptic		
		Portico	Evolut R	*p*-value	Portico	Evolut R	*p*-value
No. of patients	374 (100%)	28 (100%)	79 (100%)	–	83 (100%)	184 (100%)	–
Femoral route	343 (91.7%)	25 (89.3%)	73 (92.4%)	0.69	71 (85.5%)	174 (94.6%)	0.013
Oversizing (%)	18.9±7.1	15.9±5.7	19.5±6.9	0.032	16.6±5.3	20.1±9.5	0.15
Predilatation	139 (37.2%)	16 (57.1%)	24 (30.4%)	0.012	44 (53.0%)	55 (29.9%)	<0.001
Implantation depth NCC (mm)	3.6±1.8	4.6±1.5	3.6±1.8	0.039	4.4±2.0	3.2±1.7	<0.001
Implantation depth LCC (mm)	4.3±1.8	4.8±1.7	3.9±1.3	0.017	5.2±2.1	4.0±1.8	<0.001
Post-dilatation	170 (45.4%)	13 (46.4%)	36 (45.5%)	1.00	37 (44.6%)	84 (45.7%)	0.57
Vascular complication	30 (8.0%)	2 (7.1%)	4 (5.1%)	0.65	10 (12.0%)	14 (7.6%)	0.24
Emergent cardiac surgery	3 (0.9%)	0 (0.0%)	0 (0.0%)	–	2 (2.4%)	1 (0.5%)	0.23
Need for second valve	4 (1.1%)	0 (0.0%)	0 (0.0%)	–	1 (1.2%)	3 (1.6%)	1.00
Mean gradient (mmHg)	7.7±3.7	7.5±3.7	7.2±4.2	0.79	8.3±3.4	7.7±3.6	0.22
PVL absent/trivial	125 (33.4%)	12 (42.9%)	21 (26.6%)	0.11	25 (30.1%)	67 (36.4%)	0.32
PVL mild	219 (58.6%)	16 (57.1%)	46 (58.2%)	0.92	50 (60.2%)	107 (58.2%)	0.75
PVL moderate/severe	30 (8.0%)	0 (0.0%)	12 (15.2%)	0.034	8 (9.6%)	10 (5.4%)	0.21
PM implantation	67 (17.9%)	5 (17.9%)	22 (27.8%)	0.30	9 (10.8%)	31 (16.8%)	0.20
30-day mortality	16 (4.3%)	1 (3.6%)	5 (6.3%)	1.00	2 (2.4%)	8 (4.3%)	0.73

LCC: left coronary cusp; NCC: non-coronary cusp; PVL: paravalvular leak

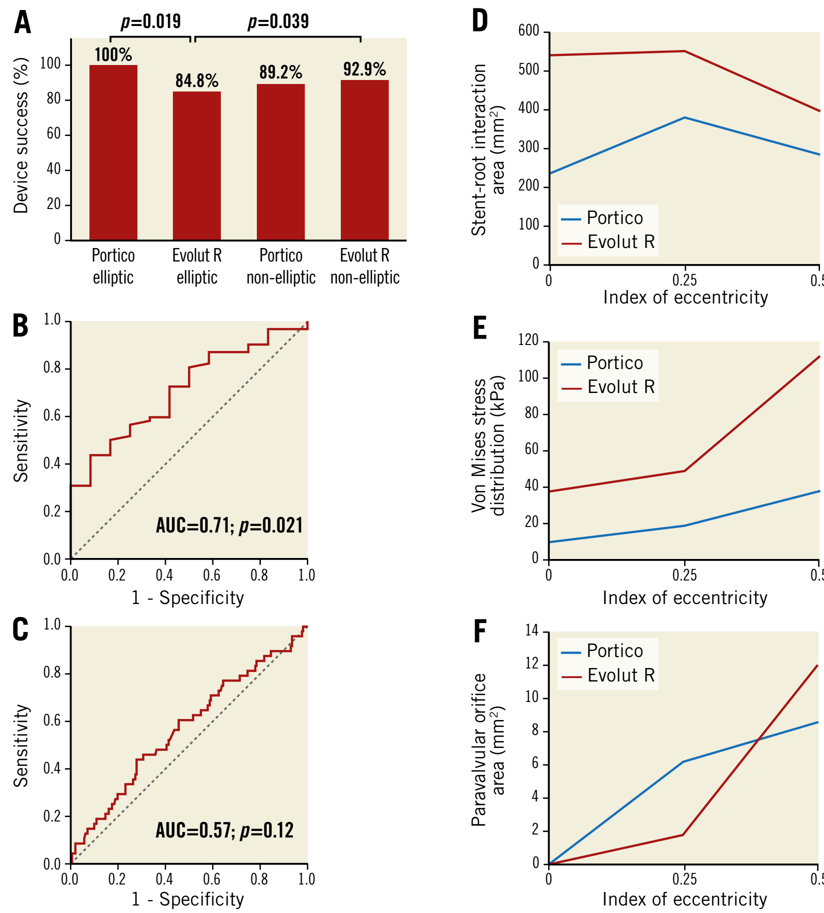

Figure 1. *Device success and simulation post-processing. A) Device success rates; capability of the index of eccentricity to predict device success in the Portico (B) and device non-success in the Evolut R group (C). Stent-root interaction area (D), stress distribution (E) and paravalvular orifice area (F) of the Portico and Evolut R.*

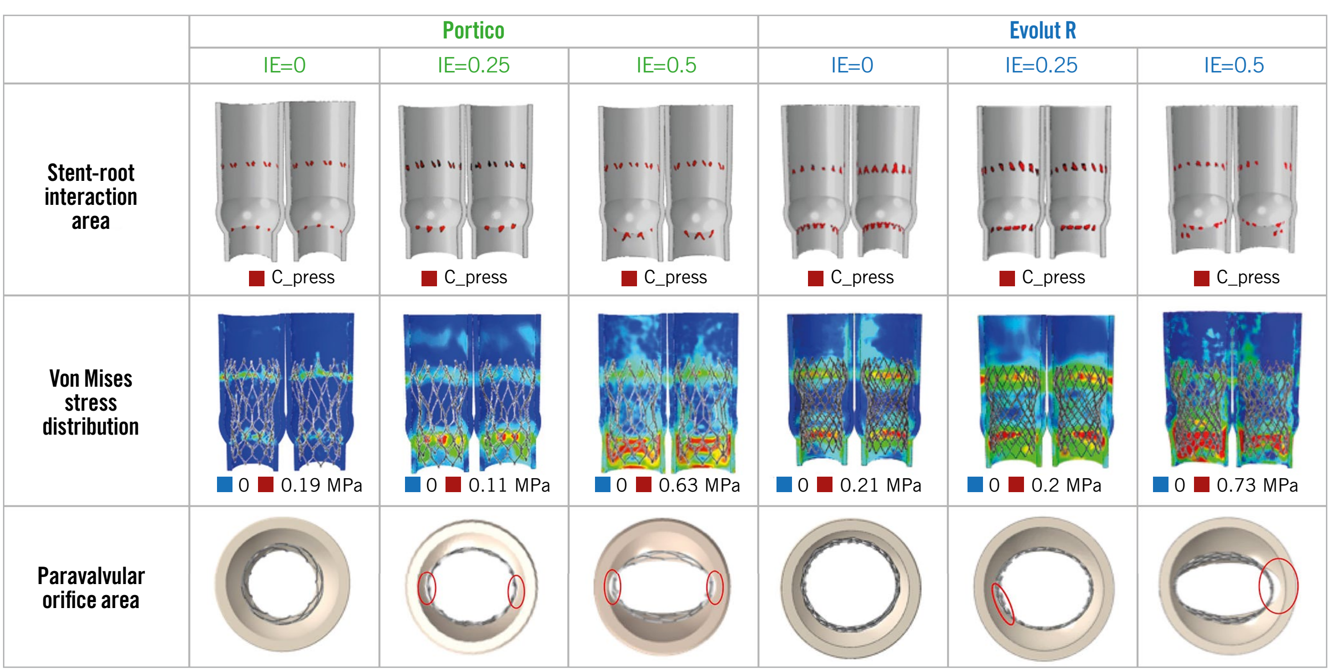

Figure 2. *Simulation analysis.*

On computational simulation, the small paravalvular orifice area observed with the Portico in very elliptic annuli resulted from a better compliance of the stent frame to the aortic annulus, probably related to its cells which are larger than those of the Evolut R. Large cells reduce the radial force of the Portico, which is approximately one-third that of the Evolut R, but increase its conformability, providing optimal sealing when eccentricity is pronounced **(Supplementary Figure 4, Supplementary Figure 5)**. Conversely, when eccentricity is mild (IE=0.25), the greater radial force of the Evolut R may compensate for its lower compliance.

Simulation findings seemed consistent with the clinical data with respect to ≥moderate PVL for Evolut R elliptic versus non-elliptic annulus patients and Portico versus Evolut R elliptic ones. Notably, the higher ≥moderate PVL rate in Portico non-elliptic versus elliptic annulus patients (9.6% vs 0.0%; p=0.20) may be due to the greater but still not significant calcium volume in this group, despite a similar implantation depth **(Supplementary Table 1-Supplementary Table 4)**.

Prosthesis function was comparable between the Portico and Evolut R even by IE >0.30 (6.2±1.6 mmHg vs 7.5±3.9 mmHg; p=0.46) despite the intra-annular valve position of the Portico.

Limitations

The number of Portico and Evolut R patients was not perfectly balanced due to our institutional policy (Evolut R was used in half of the procedures) and to the 0.25 cut-off to define ellipticity in order to provide a better insight into an uncommon but still complex population[1]. Additionally, the low number of events prevented multivariate analysis.

Conclusions

In patients with an elliptic annulus, implantation of the Portico valve showed excellent ≥moderate PVL and device success rates, compared to the Evolut R. This may be due to the high conformability of the Portico to elliptic geometry.

Acknowledgements

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Impact on daily practice

In elliptic annulus patients, the Portico valve showed optimal conformability, lower ≥moderate PVL and higher device success rates than the Evolut R.

Conflict of interest statement

F. Bedogni and F. De Marco are consultants for Medtronic and Abbott. N. Brambilla is a consultant for Abbott. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. Statistical analysis.

Supplementary Figure 1. Study flow chart.

Supplementary Figure 2. The Evolut R and Portico devices.

Supplementary Figure 3. Idealised aortic root models.

Supplementary Figure 4. Case example.

Supplementary Figure 5. Case example.

Supplementary Table 1. Characteristics of patients with >moderate PVL.

Supplementary Table 2. Procedural data of elliptic versus non-elliptic annulus patients.

Supplementary Table 3. Echocardiography and CT-angiography data of Portico and Evolut R patients.

Supplementary Table 4. Calcium volume 850 HU in Portico/Evolut R versus elliptic/non-elliptic annulus patients.

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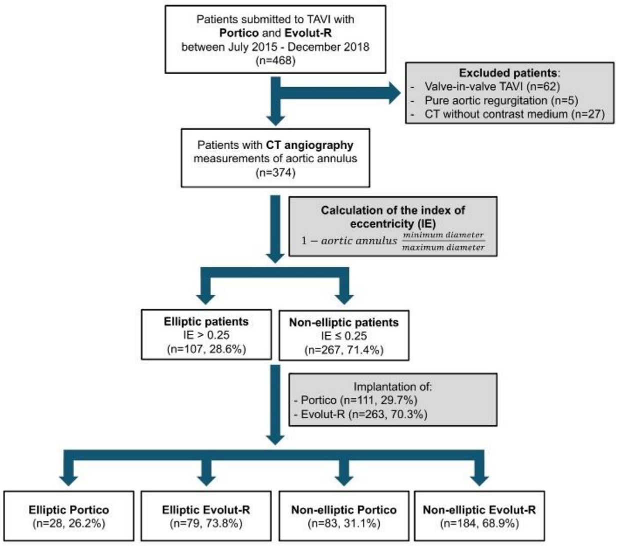
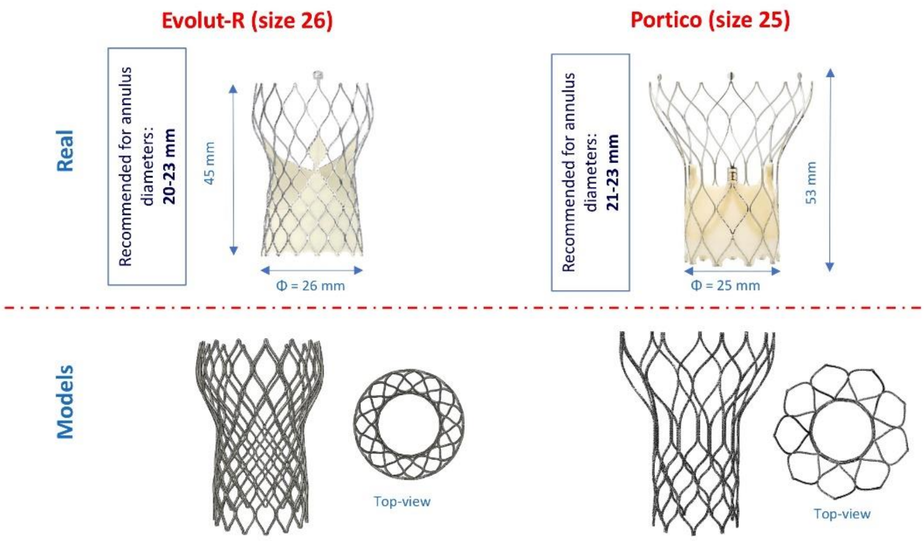
Supplementary data

Supplementary Appendix 1. Statistical analysis

Data are shown as frequencies and percentages for categorical variables and as mean±standard deviation for normally distributed continuous variables. Median and interquartile range are provided for non-normally distributed variables. Comparisons of categorical variables were made with the two-sided chi-square test or, when the expected event rate was <5, with the two-sided Fisher's exact test. Continuous variables were compared using the unpaired two-sided Student's t-test for normally distributed variables and a Mann-Whitney U test for non-normally distributed variables. Receiver operating characteristic (ROC) analysis was used to determine the predictive value of the index of eccentricity for device success. P-values <0.05 were considered statistically significant. Analyses were performed using SPSS, Version 22.0 (IBM Corp., Armonk, NY, USA).

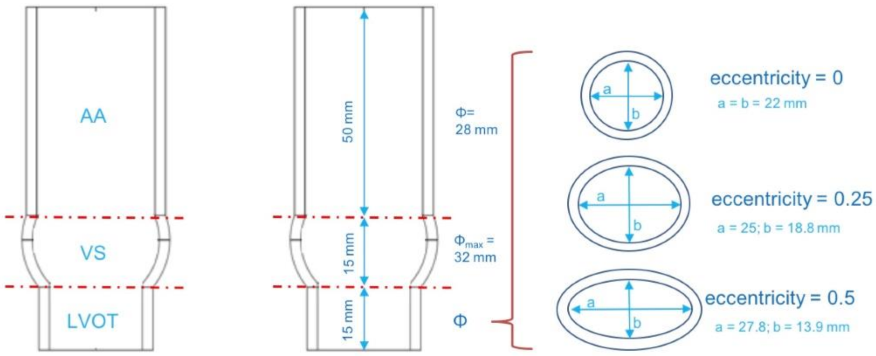


Supplementary Figure 1. Study flow chart.



Supplementary Figure 2. The Evolut R and Portico devices.

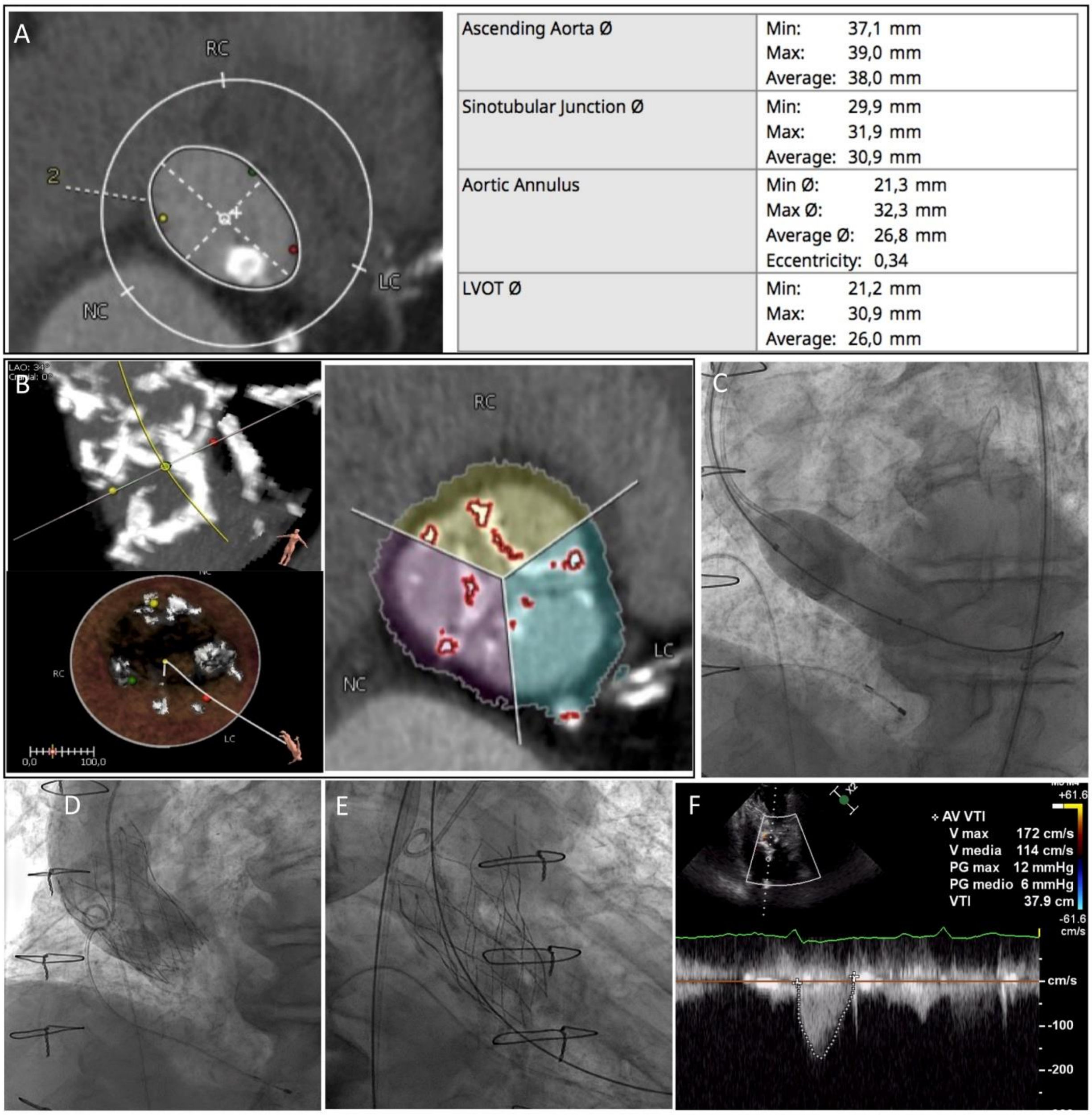
Models for computational simulation are displayed.



Supplementary Figure 3. Idealised aortic root models.

Three different indices of eccentricity (IE=0, 0.25, 0.5) are displayed.

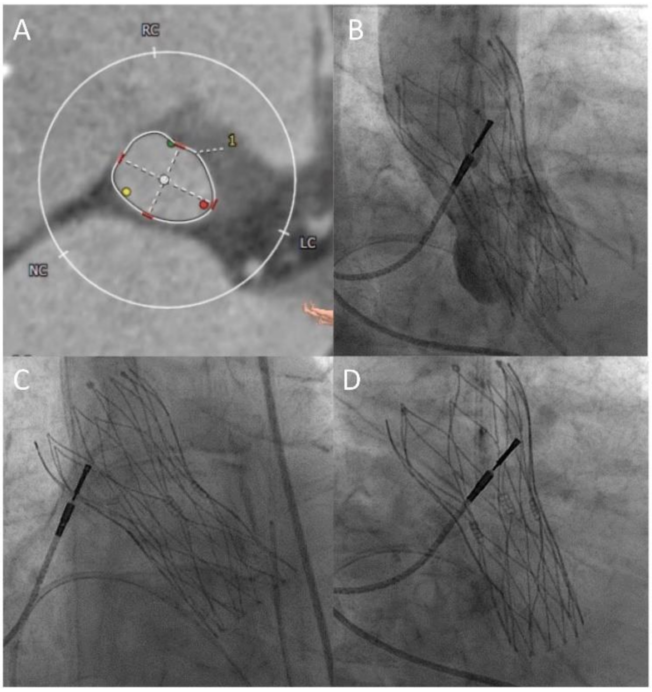
AA: ascending aorta; LVOT: left ventricular outflow tract; VS: sinus of Valsalva



Ascending Aorta Ø	Min: 37,1 mm Max: 39,0 mm Average: 38,0 mm
Sinotubular Junction Ø	Min: 29,9 mm Max: 31,9 mm Average: 30,9 mm
Aortic Annulus	Min Ø: 21,3 mm Max Ø: 32,3 mm Average Ø: 26,8 mm Eccentricity: 0,34
LVOT Ø	Min: 21,2 mm Max: 30,9 mm Average: 26,0 mm

Supplementary Figure 4. Case example.

A) CT angiography of an 87-year-old patient with a severely elliptic aortic annulus (IE=0.34). B) Calcium volume (850 HU) at the level of the aortic leaflets showing moderately extended calcifications (551.7 mm^3). C) Predilatation with a 23x45 mm semi-compliant balloon. D) Final angiography (CAU 8°/LAO 35°) showing correct positioning of Portico 29 mm valve with no paravalvular leak. E) Contralateral view (CAU 7°/RAO 24°) showing the compressed shape of the Portico inside the aortic annulus. F) Transthoracic echocardiography showing optimal mean aortic gradients.



Supplementary Figure 5. Case example.

A) CT angiography of an 80-year-old patient with elliptic aortic annulus (min diameter 15.0 mm, max diameter 20.3 mm, perimeter 58 mm, IE=0.26). B) Final angiography (CAU 12°/LAO 14°) showing correct positioning of Portico 25 mm valve with no paravalvular leak. Implantation projection (CAU 12°/LAO 14°) (C) and contralateral view (CAU 19°/RAO 35°) (D) show the high conformability of the Portico to the elliptic aortic annulus.

Supplementary Table 1. Characteristics of patients with ≥moderate PVL.

	Overall (N=374, 100%)			≥mod PVL (N=30, 100%)		
Variables	**≥mod PVL (+)**	**≥mod PVL (-)**	***p*-value**	**Portico**	**Evolut R**	***p*-value**
No. of patients	30 (8.0%)	344 (92.0%)	-	8 (26.7%)	22 (73.3%)	-
Annulus mean diameter (mm)	23.7±2.9	23.4±2.4	0.70	24.3±1.9	23.5±3.1	0.51
Index of eccentricity	0.23±0.08	0.21±0.07	0.16	0.20±0.03	0.24±0.09	0.049
Annulus perimeter (mm)	75.3±8.9	74.1±7.8	0.42	76.5±5.8	74.9±9.8	0.67
Calcium volume 850 HU (mm^3)	381.5 [166.3-568.9]	207.8 [128.5-378.9]	0.034	297.3 [224.3-405.0]	472.1 [155.0-669.4]	0.21
Degree of oversizing (%)	18.0±9.4	19.0±15.5	0.72	12.0±2.9	20.0±10.0	0.034
Implantation depth LCC (mm)	4.3±1.9	3.6±1.5	0.044	4.6±2.4	2.8±1.6	0.032
Implantation depth NCC (mm)	3.7±1.8	3.2±2.0	0.20	4.6±1.7	3.3±1.3	0.046
Predilatation	11 (36.7%)	128 (37.2%)	0.95	4 (50.0%)	7 (31.8%)	0.42
Post-dilatation	18 (60.0%)	152 (44.2%)	0.095	3 (37.5%)	15 (68.2%)	0.21

LCC: left coronary cusp; NCC: non-coronary cusp

Supplementary Table 2. Procedural data of elliptic versus non-elliptic annulus patients.

	Elliptic (IE >0.25)	**Non-elliptic (IE $\leq$0.25)**	***p*-value**
No. of patients	107	267	-
Predilatation	40 (37.4%)	99 (37.1%)	0.96
Post-dilatation	49 (45.8%)	121 (45.3%)	0.93
Oversizing (%)	18.7±6.8	19.0±14.2	0.84
Implantation depth NCC (mm)	3.8±1.7	3.6±1.8	0.33
Implantation depth LCC (mm)	4.1±1.4	4.4±2.0	0.20

LCC: left coronary cusp; NCC: non-coronary cusp

Supplementary Table 3. Echocardiography and CT-angiography data of Portico and Evolut R patients.

Variables	**Portico**	**Evolut R**	***p*-value**
No. of patients	111	263	-
Ejection fraction (%)	54.6±10.2	52.5±10.9	0.13
Mean aortic gradient (mmHg)	44.2±15.7	44.8±17.1	0.81
Aortic regurgitation ≥moderate	23 (20.7%)	56 (21.3%)	0.90
Left main height (mm)	14.3±3.2	15.1±3.6	0.10
Right coronary artery height (mm)	17.6±3.6	18.4±4.1	0.14
Annulus mean diameter (mm)	23.1±2.0	23.6±2.6	0.12
Annulus max diameter (mm)	25.8±2.4	26.6±2.9	0.021
Annulus min diameter (mm)	20.4±2.1	20.6±2.8	0.31
Index of eccentricity	0.21±0.07	0.22±0.07	0.19
Annulus perimeter (mm)	72.7±7.5	74.8±8.0	0.025
Annulus area (mm^2)	379.2±132.9	431.0±105.5	<0.001
Sinus of Valsalva diameter (mm)	31.2±3.3	33.0±18.4	0.39
Calcium volume 850 HU (mm^3)	224.3 [107.9-406.5]	220.0 [134.6-401.1]	0.78

Supplementary Table 4. Calcium volume 850 HU in Portico/Evolut R versus elliptic/non-elliptic annulus patients.

Calcium volume 850 HU (mm^3)	Portico	Evolut R	*p*-value
Elliptic	122.6 [51.9–384.4]	205.5 [102.7–425.4]	0.56
Non-elliptic	274.7 [132.3-420.8]	220.1 [144.0-385.0]	0.88
***p*-value**	0.32	0.31	-