Transcatheter Replacement of Failed Bioprosthetic Valves

Large Multicenter Assessment of the Effect of Implantation Depth on Hemodynamics After Aortic Valve-in-Valve

Matheus Simonato; John Webb, MD; Ran Kornowski, MD; Alec Vahanian, MD; Christian Frerker, MD; Henrik Nissen, MD; Sabine Bleiziffer, MD; Alison Duncan, MD; Josep Rodés-Cabau, MD; Guilherme F. Attizzani, MD; Eric Horlick, MD; Azeem Latib, MD; Raffi Bekeredjian, MD; Marco Barbanti, MD; Thierry Lefevre, MD; Alfredo Cerillo, MD; José María Hernández, MD; Giuseppe Bruschi, MD; Konstantinos Spargias, MD; Alessandro Iadanza, MD; Stephen Brecker, MD; José Honório Palma, MD; Ariel Finkelstein, MD; Mohamed Abdel-Wahab, MD; Pedro Lemos, MD; Anna Sonia Petronio, MD; Didier Champagnac, MD; Jan-Malte Sinning, MD; Stefano Salizzoni, MD; Massimo Napodano, MD; Claudia Fiorina, MD; Antonio Marzocchi, MD; Martin Leon, MD; Danny Dvir, MD

Background—Transcatheter valve implantation inside failed bioprosthetic surgical valves (valve-in-valve [ViV]) may offer an advantage over reoperation. Supra-annular transcatheter valve position may be advantageous in achieving better hemodynamics after ViV. Our objective was to define targets for implantation that would improve hemodynamics after ViV.

Methods and Results—Cases from the Valve-in-Valve International Data (VIVID) registry were analyzed using centralized core laboratory assessment blinded to clinical events. Multivariate analysis was performed to identify independent predictors of elevated postprocedural gradients (mean ≥20 mm Hg). Optimal implantation depths were defined by receiver operating characteristic curve. A total of 292 consecutive patients (age, 78.9±8.7 years; 60.3% male; 157 CoreValve Evolut and 135 Sapien XT) were evaluated. High implantation was associated with significantly lower rates of elevated gradients in comparison with low implantation (CoreValve Evolut, 15% versus 34.2%; *P*=0.03 and Sapien XT, 18.5% versus 43.5%; *P*=0.03, respectively). Optimal implantation depths were defined: CoreValve Evolut, 0 to 5 mm; Sapien XT, 0 to 2 mm (0–10% frame height); sensitivities, 91.3% and 88.5%, respectively. The strongest independent correlate for elevated gradients after ViV was device position (high: odds ratio, 0.22; confidence interval, 0.1–0.52; *P*=0.001), in addition to type of device used (CoreValve Evolut: odds ratio, 0.5; confidence interval, 0.28–0.88; *P*=0.02) and surgical valve mechanism of failure (stenosis/mixed baseline failure: odds ratio, 3.12; confidence interval, 1.51–6.45; *P*=0.002).

Conclusions—High implantation inside failed bioprosthetic valves is a strong independent correlate of lower postprocedural gradients in both self- and balloon-expandable transcatheter valves. These clinical evaluations support specific implantation targets to optimize hemodynamics after ViV. **(*Circ Cardiovasc Interv*. 2016;9:e003651. DOI: 10.1161/CIRCINTERVENTIONS.115.003651.)**

Key Words: aortic valve ■ bioprosthesis ■ hemodynamics ■ multivariate analysis ■ transcatheter aortic valve replacement

Received November 17, 2015; accepted April 29, 2016.

From the Centre for Heart Valve Innovation, Department of Cardiology, St. Paul's Hospital, Vancouver, Canada (M.S., J.W., D.D.); Division of Cardiovascular Surgery, Escola Paulista de Medicina—UNIFESP, São Paulo, Brazil (M.S., J.H.P.); Interventional Cardiology Institute, Cardiology Department, Rabin Medical Center, Petah Tivka, Israel (R.K.); Cardiology Department, Hôpital Bichat-Claude Bernard, Paris, France (A.V.); Department of Cardiology, Asklepios Klinik, Hamburg, Germany (C. Frerker); Department of Cardiology, Odense University Hospital, Denmark (H.N.); Department of Cardiovascular Surgery, Deutsches Herzzentrum München, Munich, Germany (S. Bleiziffer); Echocardiography Service, Royal Brompton and Harefield, London, United Kingdom (A.D.); Québec Heart and Lung Institute, Laval University, Québec City, Canada (J.R.-C.); Cardiovascular Imaging Core Laboratory, Case Western Research University, Cleveland, OH (G.F.A.); Peter Munk Cardiac Centre, University Health Network, University of Toronto, Canada (E.H.); Cardiologia Interventistica ed Emodinamica, Ospedale San Raffaele, Milan, Italy (A.L.); Kardiologie, Angiologie und Pneumologie, Zentrum für Innere Medizin, Universitätsklinikum Heidelberg, Germany (R.B.); Division of Cardiology, Ospedale Ferrarotto, Catania, Italy (M.B.); Institut Cardiovasculaire Paris Sud, Hôpital Jacques Cartier, Massy, France (T.L.); Fondazione Toscana Gabriele Monasterio, L'Ospedale del Cuore G. Pasquinucci, Massa, Italy (A.C.); Unidad de Hemodinámica y Cardiologia Intervencionista, Hospital Universitario Virgen de la Victoria, Malaga, Spain (J.M.H.); Dipartimento Cardiotoracovascolare, Ospedale Niguarda Ca' Granda, Milan, Italy (G.B.); Transcatheter Heart Valve Department, Hygeia Hospital, Athens, Greece (K.S.); UOC Emodinamica—Dipartimento Cardio Toracico, Azienda Ospedaliera Universitaria Senese, Siena, Italy (A.I.); Cardiac Catheterisation Laboratories, St. George's Hospital, London, United Kingdom (S. Brecker); Cardiac Catheterization Unit, Division of Cardiology, Tel Aviv Sourasky Medical Center, Israel (A.F.); Herzzentrums der Segeberger Kliniken, Segeberger Kliniken, Bad Segeberg, Germany (M.A.-W.); Serviço de Hemodinâmica e Cardiologia Intervencionista do Instituto do Coração, Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo, Brazil (P.L.); Laboratorio di Emodinamica, Università di Pisa, Italy (A.S.P.); Cardiologie Interventionnelle, Clinique du Tonkin, Villeurbanne, France (D.C.); Medizinische Klinik II—Innere Medizin (Kardiologie, Angiologie und Pneumologie), Universitätsklinikum Bonn, Germany (J.-M.S.); Department of Cardiovascular and Thoracic Surgery, Città della Salute e della Scienza—Molinette Hospital, Torino, Italy (S.S.); Department of Cardiac Thoracic and Vascular Sciences, Università degli Studi di Padova, Italy (M.N.); Cardiothoracic and Vascular Department, Spedali Civili di Brescia, Italy (C. Fiorina); Institute of Cardiology, Policlinico Sant'Orsola Malpighi, Bologna, Italy (A.M.); and Center for Interventional Vascular Therapy, Columbia University Medical Center, New York, NY (M.L.).

Correspondence to Danny Dvir, MD, St Paul's Hospital, 1081 Burrard St, Vancouver, Canada V6Z 1Y6. E-mail danny.dvir@gmail.com

WHAT IS KNOWN

- Transcatheter heart valve implantation inside failed aortic surgical bioprosthetic valves (valve-in-valve) represents an appealing less invasive alternative to reoperation.
- A major limitation of valve-in-valve implantation is transcatheter heart valve underexpansion, resulting in elevated postprocedural gradients.
- Supra-annular transcatheter heart valve device position may be advantageous in achieving better leaflet function and hemodynamics after valve-in-valve.

WHAT THE STUDY ADDS

- Study results demonstrate the importance of high-device position for achieving optimal hemodynamics postprocedure and support specific implantation targets for different transcatheter heart valve devices during valve-in-valve procedures.
- Optimal implantation depths could be defined as 0 to 5 mm for CoreValve Evolut and 0 to 2 mm (0%–10% device frame) for Sapien XT.

The majority of surgical valves currently implanted are bioprostheses because of less thrombotic complications when compared with mechanical heart valves.[1] However, these tissue valves have limited durability and commonly fail within 10 to 15 years.[2–4] Patients with failed surgical bioprosthetic valves are frequently at high risk because of old age, comorbidities, and the need to repeat their cardiac surgery.[5–8] Transcatheter heart valve (THV) implantation inside failed aortic surgical bioprosthetic valves (valve-in-valve [ViV]) represents an appealing less invasive alternative to reoperation.[9,10]

A major limitation of ViV implantation is THV underexpansion because of the nonelastic physical characteristics of the surgical valve ring. As a result, elevated postprocedural gradients and severe prosthesis–patient mismatch (PPM) are common.[10,11] Suboptimal THV leaflet coaptation, leaflet-frame contact, and poor hemodynamics after ViV implantation could impair device durability, which is a concern especially in patients with reasonable life expectancy.[12] Therefore, it is widely agreed that operators of ViV procedures should aim for lower gradients. Supra-annular THV device position may be advantageous in achieving better leaflet function and hemodynamics after ViV.[13] THV leaflets, when positioned above the failed surgical valve ring, would be expected to operate unencumbered by the nonelastic portion of the original surgical valve.

Each THV device has specific physical characteristics and geospatial relationships to the annulus. Some devices will act more supra-annular than others, even when implanted in the same depth below the surgical valve ring. Nevertheless, it is possible that all THV devices, even those considered intra-annular, will be less constrained by the original surgical valve if implanted higher. However, aiming for the highest possible device position may result in a substantial risk for THV malposition or migration. Therefore, there is an urgent clinical need to define the optimal zone for THV implantation in ViV procedures.

The aim of the current investigation was to validate the hypothesis that higher THV implantation would be associated with improved hemodynamics in aortic ViV. In addition, we aimed to define implantation depth targets that would allow for optimal hemodynamics after the procedure, using different THV devices.

Methods

Registry Design

The Valve-in-Valve International Data (VIVID) registry is a global registry of ViV procedures, which is inclusive of different THV devices and valve positions.[10] Since 2010, the registry prospectively collected data from centers in Europe, North America, South America, Africa, Oceania, and the Middle East. Collection used a dedicated case report form. In the following analysis, only cases performed in the aortic position and using the most commonly used THVs for ViV, namely the CoreValve/Evolut (Medtronic, Minneapolis, MN) and Sapien/Sapien XT (Edwards Lifesciences, Irvine, CA), were included. ViV cases performed using other THV devices or implanted in nonaortic positions were excluded from the current analysis. Inconsistencies were resolved directly with local investigators and on-site data monitoring. All patients gave written informed consent to a transcatheter aortic ViV procedure. A local ethics committee approved the inclusion of patients in each center.

Definitions

Patient operative mortality risk after surgical valve replacement was calculated using conventional scores. The mechanism of bioprosthetic valve failure (ie, regurgitation, stenosis, or combined) was evaluated using criteria set by the American Society of Echocardiography.[14] Patients with at least a moderate degree of both stenosis and regurgitation were included in the combined group. Other patients were categorized according to the primary mechanism of failure, either stenosis or regurgitation. Body surface area was calculated using the Mosteller formula. PPM of the surgical valve was determined by using reference effective orifice area values specific for each model and label size. Similarly, PPM of the THV device was calculated by using the effective orifice area measured after ViV. Moderate PPM was defined as indexed effective orifice area between 0.65 and 0.85 cm^2/m^2 for nonobese patients (body mass index <30 kg/m^2) and 0.55 and 0.7 cm^2/m^2 for obese (body mass index ≥30 kg/m^2) ones. Severe PPM was defined as indexed effective orifice area ≤0.65 cm^2/m^2 for nonobese individuals and indexed effective orifice area ≤0.55 cm^2/m^2 for obese ones. Major clinical end points were assessed according to the Valve Academic Research Consortium II (VARC II) criteria.[15] Early postimplantation hemodynamic data were obtained from either intraprocedural or first postprocedural echocardiogram. Elevated gradients were defined as those having mean gradient ≥20 mm Hg.[15]

Implantation Depth Assessment

Centralized core laboratory assessment of implantation depth was performed by an experienced operator blinded to all clinical results (St. Paul's Hospital, Vancouver, Canada). Fluoroscopic images were obtained from each selected case after the THV was implanted in its final position. A total of 407 consecutive cases were received from participant centers. High-magnification images with reasonable resolution and perpendicularity to both the THV device and the surgical valve were selected. Cases with inadequate quality, perpendicularity, or essential missing information (n=27) were excluded. ViV procedures using more than one THV (n=3), or performed in stentless surgical valves (n=41), or in stented surgical valves with rings that do not include fluoroscopic markers (eg, Medtronic Mosaic; n=44) were excluded as well, due to lack of reliable reference for implantation

depth. Due to lack of reliable reference for implantation depth. A total of 292 cases were available for analysis (age, 78.9±8.7 years; 60.3% male; 157 CoreValve Evolut and 135 Sapien XT). Depths of implantation were assessed in relation to the ventricular border of the surgical valve ring. THV devices positioned below the surgical valve ring were defined as having a positive depth and, in rare situations, THVs implanted above the surgical valve ring were defined as having a negative depth.

The bottom diamond of the CoreValve Evolut was used as the reference for the creation of a scale. One straight line was traced on each side of the device. The 2 values obtained were added together, and their average was considered the final depth of implantation for each case (Figure 1). With regard to Sapien XT, 1 straight line was traced on each side of the device. The values obtained were added, and their average was considered the height of the device. Another line was traced at each side of the THV, starting from the surgical valve ring to the bottom of the THV. The values from both lines were added, and their average was considered the depth numeric value. Finally, the depth was then defined as the percentage of the THV height below the stented surgical valve ring (Figure 1). Device height in millimeters was estimated by multiplying the depth value by the height of the expanded device (14 mm for the 23-mm device, 17 mm for the 26-mm device, and 19 mm for the 29-mm device).

Statistical Analysis

Results are presented as mean±SD for continuous variables with normal distribution, median (interquartile range) for continuous variables without normal distribution, and number (percentage) for categorical data. A receiver operating characteristic curve was performed for each data set to establish the implantation depth having the highest combined sensitivity and specificity. Subsequently, cases were stratified into high- and low-implantation groups. Student *t* test was used to compare normally distributed continuous variables between the high-implantation and the low-implantation groups for each THV device. Mann–Whitney *U* test was used for non-normally distributed variables. χ^2 and Fisher exact tests were used to compare categorical variables. Time-to-event curves were calculated using the Kaplan–Meier method, and results were compared using the log-rank statistic. For multivariable analysis of predictors for high postprocedural gradients, a logistic regression was used. The initial selection of variables entered into the univariate model included the following: sex, age, mechanism of failure, left ventricular ejection fraction (LVEF), bioprosthetic type (stented versus stentless), small surgical valve (label size ≤21 mm), and the device used during the VIV procedure (CoreValve Evolut versus Sapien XT). Variables with $P<0.10$ in the univariate analysis were further examined in a stepwise model. The results of the multivariate analysis are presented as odds ratio (OR) with 95% confidence interval (CI). Elevated postprocedural gradient was defined as a mean gradient of at least 20 mm Hg after ViV.[15] A 2-tailed *P* value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS 22 statistical software (IBM SPSS Inc).

Results

CoreValve Evolut

Table 1 shows the baseline clinical data for 157 patients receiving CoreValve Evolut for the treatment of a failed surgical valve (age, 78.9±8.3 years; 55.4% male). Mechanism of failure distribution was as follows: 42.1% stenotic, 33.8% mixed failure, and 24.1% regurgitant. Surgical valves were small (label size ≤21 mm) in 46.5% of cases. Groups were divided post hoc according to the measured depth of implantation and the observed incidence of elevated mean gradients (Figure 2). A 4.52-mm value had 91.3% sensitivity and 29.5% specificity for the occurrence of elevated postprocedural gradients. As a result, high implantation was defined as an implantation depth ≤5 mm, whereas low implantation was defined as an implantation depth >5 mm. The 2 groups had no significant differences in most baseline characteristics. The high-implantation group had higher LVEF and greater maximum gradients at baseline than the low-implantation group (Table 1). The incidence of elevated post-ViV gradients was significantly lower in the high-implantation group (15% versus 34.2%, $P=0.03$). There were no differences in mortality at 30 days or 1 year. Similarly, coronary obstruction, pacemaker need, and need for a second THV did not differ (Table 2).

Sapien XT

Table 1 shows baseline clinical data of 135 patients undergoing Sapien XT ViV implantation (age, 78.8±9.2 years; 65.9% male). Mechanism of failure distribution was as follows: 44.6% stenotic, 28.9% mixed failure, and 26.4% regurgitant. Small surgical valves (label size ≤21 mm) were present in 23% of cases. Groups were divided post hoc according to the measured depth of implantation and the observed incidence of elevated postprocedural gradients (Figure 3). An 11.8% frame depth value had 88.5% sensitivity and 32.2% specificity for the occurrence of elevated post-ViV gradients. As a result, high implantation was defined as implantation depth ≤10%, whereas low implantation was defined as an implantation depth >10%. The 2 groups had no significant differences in most baseline characteristics. The mechanism of failure differed between the groups because the high-implantation group had more cases with stenosis and small surgical valves, whereas the low-implantation group had more cases with regurgitation and large surgical valves (Table 1). The

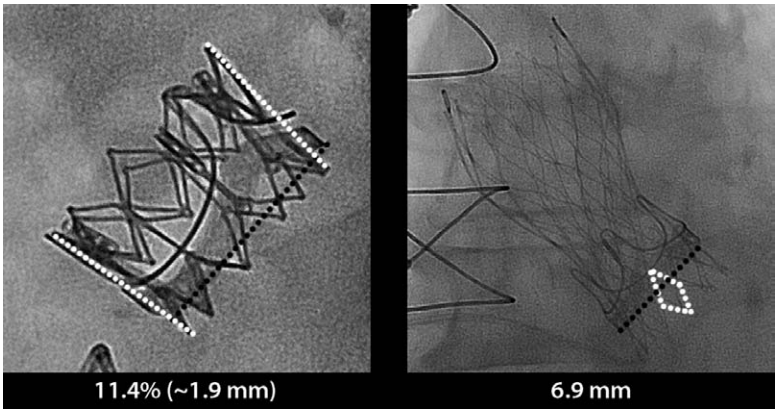

Figure 1. Depth of implantation measurement process for Sapien XT and CoreValve Evolut.

Table 1. Baseline Characteristics

Baseline	Total CoreValve (n=157)	High Implant CoreValve (n=40)	Low Implant CoreValve (n=117)	*P* Value	Total Sapien XT (n=135)	High Implant Sapien XT (n=27)	Low Implant Sapien XT (n=108)	*P* Value
Age, mean±SD, y	78.9±8.3	78.6±8.7	79.1±8.2	0.74	78.8±9.2	77.8±8.5	79.1±9.4	0.53
Male, No.	87 (55.4%)	21 (52.5%)	66 (56.4%)	0.69	89 (65.9%)	15 (55.6%)	74 (68.5%)	0.2
Height, mean±SD, cm	165.9±9.7	163.6±10	166.7±9.6	0.08	168.9±10.2	167.3±11	169.3±10	0.37
Weight, mean±SD, kg	76±16.9	73.3±15.9	76.9±17.2	0.24	74.4±15.3	76.4±18.4	74±14.5	0.48
BMI, mean±SD, kg/m^2*	27.6±6	27.2±4.6	27.7±6.4	0.65	26±4.6	27.1±5	25.8±4.5	0.18
BSA, mean±SD, m^2	1.86±0.23	1.81±0.24	1.87±0.22	0.15	1.86±0.23	1.87±0.27	1.86±0.22	0.73
Mechanism of failure				0.64				0.01
Regurgitation, No.	35 (24.1%)	8 (21.6%)	27 (25%)		32 (26.4%)	1 (5.3%)	31 (30.4%)	
Stenosis, No.	61 (42.1%)	18 (48.6%)	43 (39.8%)		54 (44.6%)	14 (73.7%)	40 (39.2%)	
Mixed, No.	49 (33.8%)	11 (29.7%)	38 (35.2%)		35 (28.9%)	4 (21.1%)	31 (30.4%)	
NYHA				0.74				0.11
I, No.	1 (0.6%)	0 (0%)	1 (0.9%)		4 (3.2%)	0 (0%)	4 (3.9%)	
II, No.	10 (6.5%)	2 (5.1%)	8 (6.9%)		6 (4.8%)	2 (8.3%)	4 (3.9%)	
III, No.	101 (65.2%)	28 (71.8%)	73 (62.9%)		85 (67.5%)	20 (83.3%)	65 (63.7%)	
IV, No.	43 (27.7%)	9 (23.1%)	34 (29.3%)		31 (24.6%)	2 (8.3%)	29 (28.4%)	
Time to failure, median (IQR), y	8 (6–12)	8 (6–12)	9 (6–11)	0.63	10 (8–13.5)	10 (8.75–13.25)	11 (8–14)	0.86
Logistic EuroSCORE,† median (IQR), %	27 (18.9–37.9)	26 (19.8–34.1)	28.4 (18–38)	0.09	23.4 (15.5–32.1)	27 (21.2–32.8)	22.9 (13.8–31.3)	0.78
EuroSCORE II,† median (IQR), %	12.9 (9.4–17.3)	12.4 (8.5–16.8)	12.9 (9.8–17.6)	0.97	11.8 (8.6–16.7)	11.8 (10–14.6)	12 (8.1–17.7)	0.97
STS† score, median (IQR), %	6.7 (4.6–14.3)	6.25 (5–16.5)	6.8 (4.6–14)	0.37	7.3 (5–10.7)	6.8 (5–10)	7.6 (5–10.8)	0.31
Diabetes mellitus, No.	45 (29.4%)	13 (33.3%)	32 (28.1%)	0.53	28 (20.7%)	11 (40.7%)	17 (15.7%)	0.004
Peripheral vascular disease, No.	29 (19%)	7 (17.9%)	22 (19.3%)	1	34 (25.4%)	7 (25.9%)	27 (25.2%)	1
Renal failure, No.‡	73 (46.5%)	17 (48.7%)	56 (47.9%)	0.56	66 (48.9%)	13 (48.1%)	53 (49.1%)	0.93
Stroke, No.	17 (10.8%)	5 (12.5%)	12 (10.3%)	0.77	15 (11.4%)	0 (0%)	15 (14.3%)	0.04
Chronic lung disease, No.	27 (20.8%)	5 (15.2%)	22 (22.7%)	0.46	18 (17.1%)	4 (18.2%)	14 (16.9%)	1
Previous permanent pacemaker, No.	19 (12.7%)	6 (16.2%)	13 (11.5%)	0.57	14 (11.6%)	2 (7.4%)	12 (12.8%)	0.73
>1 cardiac surgery, No.	20 (13%)	6 (15.8%)	14 (12.1%)	0.58	24 (20.5%)	6 (25%)	18 (19.4%)	0.58
PPM of the surgical valve§				0.76				0.68
None/moderate, No.	122 (90.4%)	31 (91.2%)	91 (90.1%)		98 (97%)	23 (95.8%)	75 (97.4%)	
Severe, No.	13 (9.6%)	3 (8.8%)	10 (9.9%)		3 (3%)	1 (4.2%)	2 (2.6%)	
Label size				0.09				0.38
≤21 mm, No.	73 (46.5%)	25 (62.5%)	48 (41%)		31 (23%)	9 (33.3%)	22 (20.4%)	
>21 mm and <25 mm, No.	48 (30.6%)	10 (25%)	38 (32.5%)		39 (28.9%)	8 (29.6%)	31 (28.7%)	
≥25 mm, No.	33 (21%)	5 (12.5%)	28 (23.9%)		62 (45.9%)	9 (33.3%)	53 (49.1%)	
Unknown, No.	3 (1.9%)	0 (0%)	3 (2.6%)		3 (2.2%)	1 (3.7%)	2 (1.9%)	
Maximum gradient, mean±SD, mm Hg	62.1±25.3	69.2±21.6	59.9±26	0.06	64.5±30	76.3±33.1	61.3±28.3	0.04

(*Continued*)

Table 1. Continued

Baseline	Total CoreValve (n=157)	High Implant CoreValve (n=40)	Low Implant CoreValve (n=117)	*P* Value	Total Sapien XT (n=135)	High Implant Sapien XT (n=27)	Low Implant Sapien XT (n=108)	*P* Value
Mean gradient, mean±SD, mm Hg	37±16.7	40.6±16	35.8±16.9	0.14	38.2±19.3	46.7±22.9	36±17.7	0.01
Aortic regurgitation (grade ≥2), No.	89 (58.2%)	18 (47.4%)	71 (61.7%)	0.12	72 (56.3%)	6 (27.3%)	66 (62.3%)	0.004
Aortic valve area, mean±SD, cm^2	0.84±0.35	0.76±0.28	0.86±0.37	0.15	0.93±0.45	0.8±0.37	0.96±0.46	0.13
Indexed aortic valve area, mean±SD, cm^2	0.45±0.2	0.42±0.15	0.46±0.21	0.31	0.5±0.24	0.41±0.15	0.52±0.25	0.01
LVEF, mean±SD, %	51.9±14.3	56.6±14.7	50.3±13.8	0.02	53.1±12.2	56.9±13.5	52.2±11.7	0.08
THV size				0.07				0.30
20 mm, No.	…	…	…		7 (5.2%)	3 (11.1%)	4 (3.7%)	
23 mm, No.	73 (47.1%)	23 (57.5%)	50 (43.5%)		78 (57.8%)	16 (59.3%)	62 (57.4%)	
26 mm, No.	73 (47.1%)	13 (32.5%)	60 (52.2%)		45 (33.3%)	8 (29.6%)	37 (34.3%)	
29 mm, No.	9 (5.8%)	4 (10%)	5 (4.3%)		5 (3.7%)	0 (0%)	5 (4.6%)	
Femoral access, No.	143 (91.7%)	37 (92.5%)	106 (91.4%)	1	83 (61.5%)	21 (77.8%)	62 (57.4%)	0.08

BMI indicates body mass index; BSA, body surface area; IQR, interquartile range; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PPM, prosthesis–patient mismatch; STS, Society of Thoracic Surgeons; and THV, transcatheter heart valve.

*Body mass index is calculated as weight (kg)/height (m^2).

†Prediction of operative mortality after conventional surgical valve replacement (STS score: http://riskcalc.sts.org/de.aspx, LogEuroSCORE: http://www.euroscore.org/calcold.html, and EuroSCORE II: http://www.euroscore.org/calc.html). Range of scores is 0% to 100%; higher score indicates greater patient risk.

‡Calculated glomerular filtration rate <60 mL/min.

§PPM of the surgical valve refers to the classification of PPM according to the reference effective orifice area of each surgical valve according to model and label size. The values refer to the implanted surgical valve before degeneration.

incidence of elevated post-ViV gradients was significantly lower in the high-implantation group (18.5% versus 43.5% in the low-implantation group, *P*=0.03). There were no differences in mortality at 30 days or 1 year or in coronary obstruction, pacemaker need, and need for a second THV (Table 2).

Multivariate Analysis

THV position was identified as the strongest correlate of elevated postprocedural gradients in multivariate analysis (high position: OR, 0.22; CI, 0.1–0.52; *P*<0.001; Figure 4). Other independent correlates were CoreValve use (OR, 0.5; CI, 0.28–0.88; *P*=0.02) and stenosis or mixed mechanism of failure (OR, 3.12; CI, 1.51–6.45; *P*=0.002). Age, male sex, LVEF, surgical valve type (stented versus stentless), and small surgical valve (≤21 mm) were not independent predictors for elevated postprocedural gradients using the current model.

Discussion

Transcatheter ViV is a less-invasive strategy that is increasingly applied to treat patients with failed bioprosthetic valves. This alternative approach is frequently limited by poor hemodynamic results.[10] This study is a comprehensive analysis of different THV devices used for ViV implantation. It supports a technical measure that can enable lower residual stenosis after ViV. There was a clear evidence of lower risk of elevated gradients with higher THV implantation (ie, more supra-annular). After this extensive analysis, optimal implantation depths could be defined: 0 to 5 mm for CoreValve Evolut and 0 to 2 mm (0%–10% device frame) for Sapien XT.

Postprocedural Gradients

The most widely recognized adverse events of ViV are malpositioning, coronary obstruction, and elevated postprocedural gradients.[16] Because physicians become more experienced with measures to avoid both malpositioning and coronary obstruction, the rates of these adverse events seem to decrease.[10] However, the concern with elevated gradients and inadequate device expansion is mainly unsolved. In the vast majority of transcatheter aortic valve replacement procedures performed in native aortic valves, final mean gradients are 5 to 10 mm Hg.[10,17] Low gradients are also commonly found in conventional surgical procedures.[18,19] In ViV, however, elevated gradients are common: the VIVID Registry previously reported an average mean gradient of 16 mm Hg.[10] In addition, severe PPM occurred in ≈30% of patients who underwent ViV.[10] Patients with baseline stenosis or those who received balloon-expandable THV devices in small surgical valves were especially prone to having poor hemodynamics after ViV.[16] PPM has several, both short- and long-term, consequences. A meta-analysis including >27 000 patients undergoing surgical aortic valve replacement and other studies have shown that both moderate and severe PPM are associated with worse outcomes.[20–22] Another concern with elevated gradients is a reduction in valve durability and increased valve degeneration.[23]

Before this study, there was no clear method for preventing this common adverse event of ViV procedures. Postdilation, for instance, may have only a limited role.[16] Several operators have attempted aggressive dilatation with some degree of success by breaking the surgical valve ring with a high-pressure balloon.[24,25]

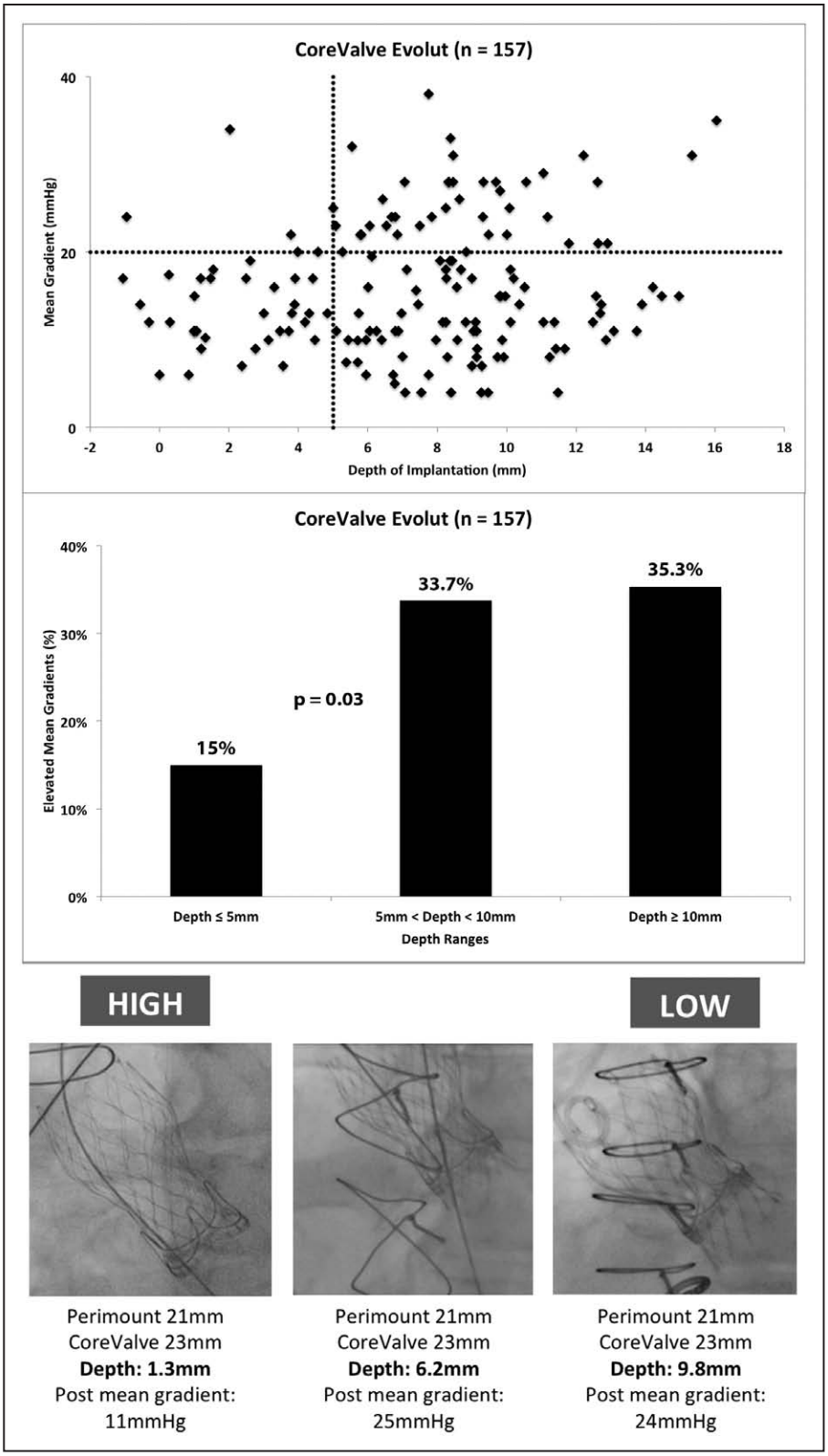

Figure 2. A total of 157 CoreValve Evolut cases with respective depths of implantation and postprocedural mean gradients. The horizontal line defines the cutoff for elevated mean gradients (≥20 mm Hg), and the vertical line demonstrates our established depth cutoff (5 mm) per receiver operating characteristic analysis. Bars demonstrate the different elevated mean gradient rates by depth of implantation range (high, middle, and low position). Examples of high, middle, and low implantation of the CoreValve Evolut are presented.

This approach, however, may involve significant risk. It seems that as long as surgical valves include nondilatable rings, a different approach is needed to ensure low gradients after ViV procedures.

Supra-Annular Positioning: A Possible Solution?

The potential advantage of supra-annularity in ViV was suggested before. Azadani et al[13] have hypothesized that it would

Table 2. Clinical Outcomes

Clinical Outcomes	Total CoreValve (n=157)	High Implant CoreValve (n=40)	Low Implant CoreValve (n=117)	*P* Value	Total Sapien XT (n=135)	High Implant Sapien XT (n=27)	Low Implant Sapien XT (n=108)	*P* Value
Duration of hospital stay, median (IQR), d	7 (5–10)	7 (5–11)	7 (5–10)	0.99	6 (4–9)	5 (3–7)	7 (4–10)	0.16
Depth of implantation, mean±SD*	7.3±3.7	2.3±1.8	9±2.5	<0.001	19.9±13.7	2.2±9.3	24.3±10.7	<0.001
Maximum gradient, mean±SD, mm Hg	28.6±13.5	26.8±10.2	29.2±14.4	0.28	33.1±13.8	31±11.3	33.5±14.4	0.49
Mean gradient, mean±SD, mm Hg	16±7.5	14.4±5.6	16.5±8.1	0.08	18.5±9.2	16±6.7	19.1±9.7	0.06
Aortic regurgitation (grade ≥2), No.	5 (3.2%)	1 (2.5%)	4 (3.4%)	1	2 (1.5%)	1 (3.7%)	1 (1%)	0.37
Aortic valve area, mean±SD, cm^2	1.52±0.5	1.5±0.41	1.52±0.52	0.82	1.31±0.38	1.26±0.22	1.32±0.41	0.36
Indexed aortic valve area,† mean±SD, cm^2/m^2	0.82±0.29	0.85±0.27	0.81±0.29	0.49	0.71±0.21	0.68±0.12	0.72±0.23	0.3
LVEF, mean±SD, %	52.7±11	55.2±9.7	51.9±11.4	0.11	51.3±11.6	55.4±11.2	50.4±11.5	0.06
30-d outcomes								
Elevated postprocedural gradient, No.	46 (29.3%)	6 (15%)	40 (34.2%)	0.03	52 (38.5%)	5 (18.5%)	47 (43.5%)	0.03
Prosthesis–patient mismatch				0.79				0.61
None/moderate, No.	78 (78%)	22 (81.5%)	56 (76.7%)		65 (63.1%)	14 (70%)	51 (61.4%)	
Severe, No.	22 (22%)	5 (18.5%)	17 (23.3%)		38 (36.9%)	6 (30%)	32 (38.6%)	
Death, No.	2 (1.3%)	0 (0%)	2 (1.7%)	1	3 (2.3%)	0 (0%)	3 (2.9%)	1
Cardiovascular death, No.	0 (0%)	0 (0%)	0 (0%)	…	3 (2.3%)	0 (0%)	3 (2.9%)	1
NYHA				0.12				1
I/II, No.	121 (87.7%)	26 (78.8%)	95 (90.5%)		96 (87.3%)	22 (88%)	74 (87.1%)	
III/IV, No.	17 (12.3%)	7 (21.2%)	10 (9.5%)		14 (12.7%)	3 (12%)	11 (12.9%)	
Major vascular complications, No.	3 (1.9%)	1 (2.5%)	2 (1.7%)	0.27	4 (3%)	1 (3.7%)	3 (2.8%)	1
Major/life-threatening bleeding complications, No.	6 (3.9%)	3 (7.5%)	3 (2.6%)	0.18	10 (7.5%)	3 (11.1%)	7 (6.5%)	0.42
Major stroke, No.	1 (0.6%)	0 (0%)	1 (0.9%)	1	2 (1.5%)	0 (0%)	2 (1.9%)	1
Acute kidney injury, No.	10 (6.5%)	6 (15%)	4 (3.5%)	0.02	8 (6%)	0 (0%)	8 (7.5%)	0.36
Coronary obstruction, No.	2 (1.3%)	0 (0%)	2 (1.7%)	1	2 (1.5%)	0 (0%)	2 (1.9%)	1
Pacemaker need, No.	7 (4.5%)	1 (2.5%)	6 (5.2%)	0.68	7 (5.6%)	2 (8%)	5 (5%)	0.63
1-y outcomes								
Death, No.	6 (3.8%)	0 (0%)	6 (5.1%)	0.19	7 (5.4%)	1 (3.8%)	6 (5.8%)	0.79
NYHA				0.54				0.29
I/II, No.	65 (83.3%)	12 (75%)	53 (85.5%)		50 (87.7%)	8 (88.8%)	42 (87.5%)	
III/IV, No.	13 (16.7%)	4 (25%)	9 (14.5%)		7 (12.3%)	1 (11.1%)	6 (12.5%)	
Maximum gradient, mean±SD, mm Hg	29.1±14.5	24±15.4	30.2±14.2	0.2	34±15.6	29.8±8.8	34.8±16.5	0.4
Mean gradient, mean±SD, mm Hg	16.1±8.9	14.2±11.5	16.6±8.1	0.39	19.7±8.8	16.9±4.5	20.2±9.2	0.33
Aortic valve area, mean±SD, cm^2	1.32±0.42	1.66±0.16	1.24±0.43	0.01	1.34±0.37	1.33±0.17	1.34±0.39	0.94

IQR indicates interquartile range; LVEF, left ventricular ejection fraction; and NYHA, New York Heart Association.
*Depth of implantation represented in mm for CoreValve and in % below surgical valve marker for Sapien XT.
†Aortic valve area (cm^2)/patient body surface area (m^2).

be possible to obtain better hemodynamic results in ViV if the THV functions above the surgical valve stent. In this way, the THV would not be constrained by the original valve. Other in-vitro assessments were performed, with similar conclusions.[26,27]

Differences in hemodynamic outcomes between CoreValve Evolut and Sapien XT with regard to ViV are probably associated with THV design and supra-annularity. The CoreValve Evolut is, essentially, a supra-annular device, as its functional part is located above the native valve annulus, whereas the Sapien XT is not.[16] This helps to explain the association between smaller surgical valves and elevated gradients that is especially common in Sapien

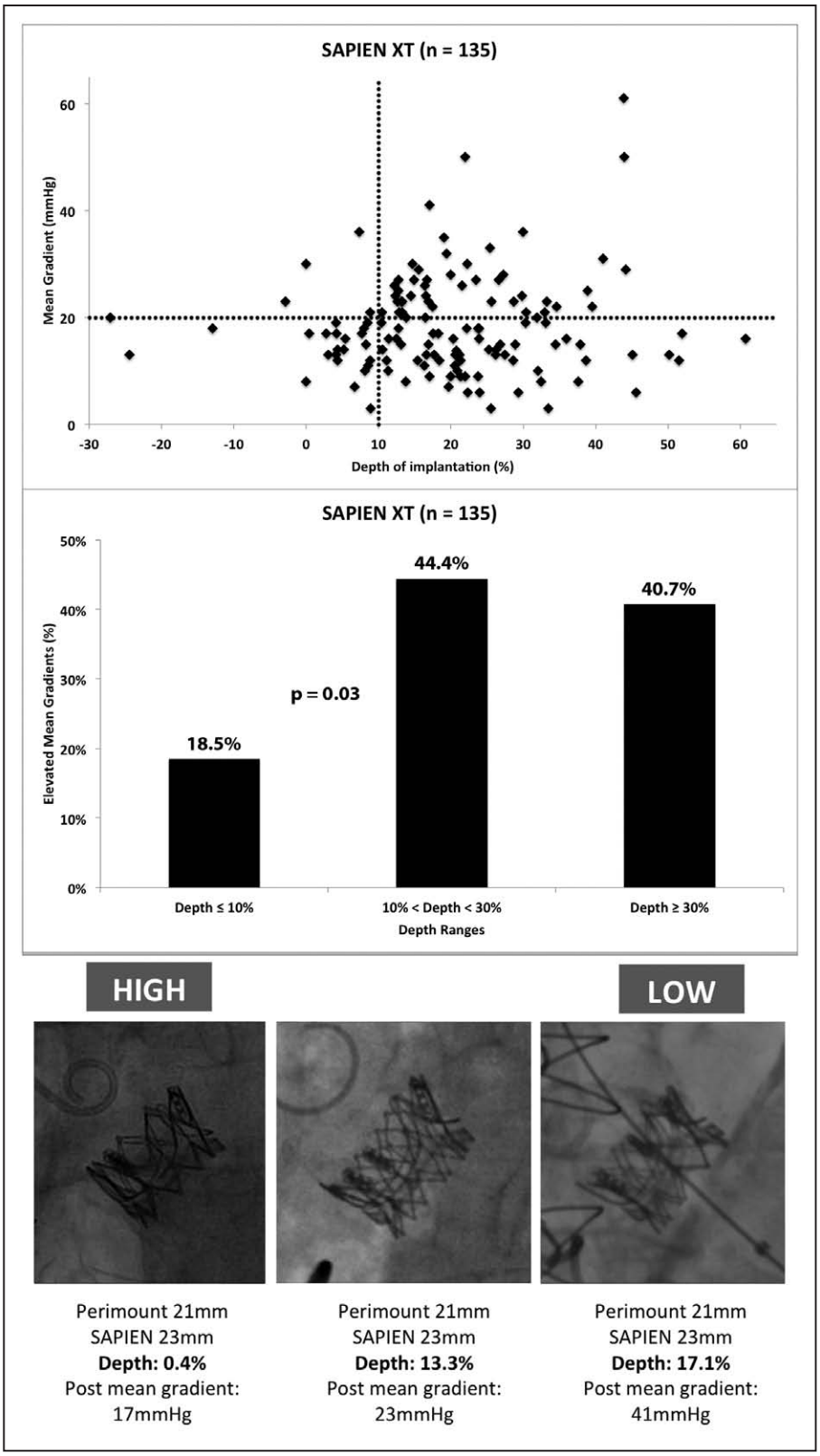

Figure 3. A total of 135 Sapien XT cases with respective implantation depths and postprocedural mean gradients. The horizontal line defines the cutoff for elevated gradients (20 mm Hg), and the vertical line demonstrates our established depth cutoff (10%) per receiver operating characteristic analysis. Bars demonstrate the different elevated mean gradient rates by depth of implantation range (high, middle, and low position). Examples of high, middle, and low implantation of the Sapien XT are presented.

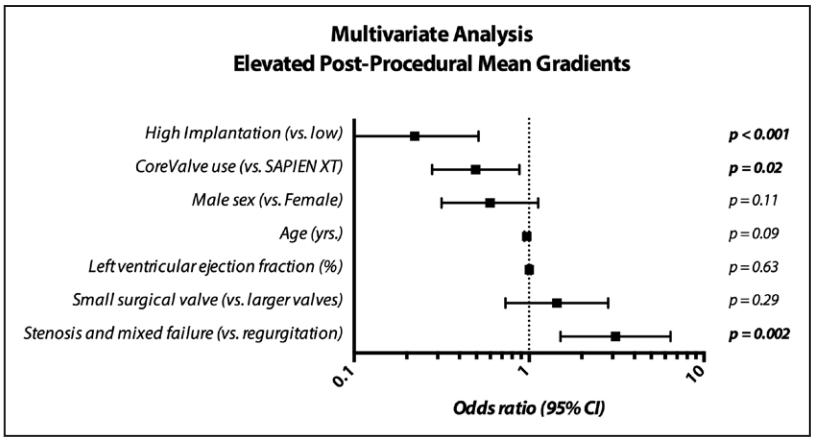

Figure 4. Multivariate analysis for correlates for elevated post–valve-in-valve mean gradients. Horizontal lines indicate 95% confidence interval (CI).

XT ViV procedures.[16] In the CoreValve Evolut, even though elevated postprocedural gradients were common as well, the same association was not present, and the relationship between surgical valves size and elevated gradients is not as robust. This suggests that other cardinal factors may be at play when it comes to post-ViV hemodynamics. According to the current analysis, it seems that implant position has a strong impact on ViV hemodynamics and is probably a major contributor to elevated gradients that was unidentified so far.

Interestingly, in the current analysis, LVEF in the high-implantation groups of both devices was higher than that in the low-implantation groups, but nevertheless the risk of having elevated postprocedural gradients was lower in the high-implantation group. In addition, the high-position Sapien XT group had worse stenosis at baseline than the low positioning one, but after ViV it showed a smaller incidence of elevated mean gradients. It can be suggested that high positioning was able to overcome the effect of the baseline stenosis and higher LVEF on elevated postprocedural gradients.

Clinical Implications: Optimal Implantation Depth in ViV

Our results suggest that higher THV implantation is important for achieving optimal hemodynamics in ViV procedures. For the CoreValve Evolut, current analysis supports that the device should be implanted in the range of 0- to 5-mm deep. For the Sapien XT, implant depth should be 0% to 10% of the device frame height (0 to ≈2 mm). Interestingly, supra-annular THV devices have longer implantation target zones than intra-annular ones. This suggests that it would be potentially more challenging to optimally position an intra-annular THV device and that large experience may be required for operators of ViV procedures with such devices.

In addition, it seems that although all patients would potentially benefit from improved hemodynamics, there are special situations that may require more attention to position the THV device. Avoiding early degeneration might be especially important in patients with small surgical valves and in relatively young patients, who could be expected to live longer and in whom long-term durability is desired. Nevertheless, excessively high implantation may put the patient at risk for THV malposition and, in rare situations, coronary flow obstruction. Physicians therefore must make clinical decisions, weighting potential risks and benefits in each case.

Limitations

Our validated centralized core laboratory method for depth measurement did not allow for depth evaluation in cases performed in stentless surgical valves and in surgical valves that lack ring fluoroscopic markers. Therefore, this may limit the application of current analysis findings about the importance of high-device positioning to stented surgical valves. The current analysis includes multiple comparisons and as a result a highly inflated false-positive rate is possible. In addition, the suggested depth cut points are data driven from the current analysis and will be validated in the future. We also note that because the vast majority of worldwide experience in ViV procedures is using Sapien XT and CoreValve Evolut, we were limited in testing the effect of implant depth using these devices. Future studies should explore next-generation THV devices with regard to their implant depth and hemodynamics after ViV procedures.

Conclusions

The current analysis is the first large comprehensive evaluation of the effect of positioning on ViV outcomes. Our results demonstrate the importance of high-device position for achieving optimal hemodynamics postprocedure and support specific implantation targets for different THV devices during ViV procedures. Other important factors for ViV hemodynamics are the type of THV used and baseline mechanism of failure.

Acknowledgments

We would like to thank the St. Paul's Foundation for their support. M. Simonato acknowledges the Science Without Borders Scholarship, provided by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and Conselho Nacional de Desenvolvimento Cientifíco e Tecnológico (CNPq), agencies of the Brazilian Federal Government.

Disclosures

Dr Dvir reports consulting for Edwards Lifesciences and Medtronic. Dr Webb reports consulting for Edwards Lifesciences. Dr Bleiziffer reports proctoring and consulting for Medtronic and proctoring for Boston Scientific and JenaValve. Dr Sinning reports receiving speaker

honoraria and research grants from Medtronic, Edwards Lifesciences, Direct Flow Medical, and Boston Scientific. Dr Barbanti reports consulting for Edwards Lifesciences. Dr Petronio reports clinical proctoring for Medtronic and Boston Scientific, membership in the Speaker's Bureau and consulting for Abbott Laboratories, Boston Scientific, Eli Lilly and Medtronic. Dr Brecker reports proctoring and consulting for Medtronic and consulting for Boston Scientific. Dr Attizzani reports consulting for St. Jude Medical, proctoring for Medtronic, and Edwards Lifesciences and membership in the Speaker's Bureau of Abbott Laboratories. Dr Latib reports consulting for Medtronic and Direct Flow Medical. Dr Spargias reports proctoring and consulting for Edwards Lifesciences, proctoring for Medtronic and St. Jude Medical. Dr Fiorina reports proctoring for St. Jude Medical and Medtronic, lecture honoraria from Edwards Lifesciences. Dr Cerillo reports proctoring for Symetis. Dr Lemos reports proctoring for Edwards Lifesciences. Dr Horlick reports consulting and program support from Edwards Lifesciences, Medtronic, and St. Jude Medical, as well as program support from Gore. Dr Vahanian reports a research grant from Edwards Lifesciences, speaker fees and honoraria from Abbott Laboratories and Valtech. Dr Abdel-Wahab reports honoraria and consulting fees from Boston Scientific, institutional research grants from St. Jude and Biotronik. Dr Bruschi reports consulting for Medtronic and Direct Flow Medical. Dr Lefèvre reports proctoring for Edwards Lifesciences. Dr Rodés-Cabau reports research grants from Edwards Lifesciences and Medtronic. The other authors report no conflicts.

References

1. Brown JM, O'Brien SM, Wu C, Sikora JA, Griffith BP, Gammie JS. Isolated aortic valve replacement in North America comprising 108,687 patients in 10 years: changes in risks, valve types, and outcomes in the Society of Thoracic Surgeons National Database. *J Thorac Cardiovasc Surg*. 2009;137:82–90. doi: 10.1016/j.jtcvs.2008.08.015.
2. Forcillo J, Pellerin M, Perrault LP, Cartier R, Bouchard D, Demers P, Carrier M. Carpentier-Edwards pericardial valve in the aortic position: 25-years experience. *Ann Thorac Surg*. 2013;96:486–493. doi: 10.1016/j.athoracsur.2013.03.032.
3. David TE, Ivanov J, Armstrong S, Feindel CM, Cohen G. Late results of heart valve replacement with the Hancock II bioprosthesis. *J Thorac Cardiovasc Surg*. 2001;121:268–277. doi: 10.1067/mtc.2001.112208.
4. Gao G, Wu Y, Grunkemeier GL, Furnary AP, Starr A. Durability of pericardial versus porcine aortic valves. *J Am Coll Cardiol*. 2004;44:384–388. doi: 10.1016/j.jacc.2004.01.053.
5. Akins CW, Buckley MJ, Daggett WM, Hilgenberg AD, Vlahakes GJ, Torchiana DF, Madsen JC. Risk of reoperative valve replacement for failed mitral and aortic bioprostheses. *Ann Thorac Surg*. 1998;65:1545–1551.
6. Maganti M, Rao V, Armstrong S, Feindel CM, Scully HE, David TE. Redo valvular surgery in elderly patients. *Ann Thorac Surg*. 2009;87:521–525. doi: 10.1016/j.athoracsur.2008.09.030.
7. Naji P, Griffin BP, Sabik JF, Kusunose K, Asfahan F, Popovic ZB, Rodriguez LL, Lytle BW, Grimm RA, Svensson LG, Desai MY. Characteristics and outcomes of patients with severe bioprosthetic aortic valve stenosis undergoing redo surgical aortic valve replacement. *Circulation*. 2015;132:1953–1960. doi: 10.1161/CIRCULATIONAHA.115.015939.
8. Kirsch M, Nakashima K, Kubota S, Houël R, Hillion ML, Loisance D. The risk of reoperative heart valve procedures in Octogenarian patients. *J Heart Valve Dis*. 2004;13:991–996.
9. Milburn K, Bapat V, Thomas M. Valve-in-valve implantations: is this the new standard for degenerated bioprostheses? Review of the literature. *Clin Res Cardiol*. 2014;103:417–429. doi: 10.1007/s00392-013-0653-3.
10. Dvir D, Webb JG, Bleiziffer S, Pasic M, Waksman R, Kodali S, Barbanti M, Latib A, Schaefer U, Rodés-Cabau J, Treede H, Piazza N, Hildick-Smith D, Himbert D, Walther T, Hengstenberg C, Nissen H, Bekeredjian R, Presbitero P, Ferrari E, Segev A, de Weger A, Windecker S, Moat NE, Napodano M, Wilbring M, Cerillo AG, Brecker S, Tchetche D, Lefèvre T, De Marco F, Fiorina C, Petronio AS, Teles RC, Testa L, Laborde JC, Leon MB, Kornowski R; Valve-in-Valve International Data Registry Investigators. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. *JAMA*. 2014;312:162–170. doi: 10.1001/jama.2014.7246.
11. Webb JG, Dvir D. Transcatheter aortic valve replacement for bioprosthetic aortic valve failure: the valve-in-valve procedure. *Circulation*. 2013;127:2542–2550. doi: 10.1161/CIRCULATIONAHA.113.000631.
12. Abbasi M, Azadani AN. Leaflet stress and strain distributions following incomplete transcatheter aortic valve expansion. *J Biomech*. 2015;48:3663–3671. doi: 10.1016/j.jbiomech.2015.08.012.
13. Azadani AN, Jaussaud N, Matthews PB, Ge L, Guy TS, Chuter TA, Tseng EE. Valve-in-valve implantation using a novel supravalvular transcatheter aortic valve: proof of concept. *Ann Thorac Surg*. 2009;88:1864–1869. doi: 10.1016/j.athoracsur.2009.08.004.
14. Zoghbi WA, Chambers JB, Dumesnil JG, Foster E, Gottdiener JS, Grayburn PA, Khandheria BK, Levine RA, Marx GR, Miller FA Jr, Nakatani S, Quiñones MA, Rakowski H, Rodriguez LL, Swaminathan M, Waggoner AD, Weissman NJ, Zabalgoitia M; American Society of Echocardiography's Guidelines and Standards Committee; Task Force on Prosthetic Valves; American College of Cardiology Cardiovascular Imaging Committee; Cardiac Imaging Committee of the American Heart Association; European Association of Echocardiography; European Society of Cardiology; Japanese Society of Echocardiography; Canadian Society of Echocardiography; American College of Cardiology Foundation; American Heart Association; European Association of Echocardiography; European Society of Cardiology; Japanese Society of Echocardiography; Canadian Society of Echocardiography. Recommendations for evaluation of prosthetic valves with echocardiography and doppler ultrasound: a report From the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2009;22:975–1014, quiz 1082. doi: 10.1016/j.echo.2009.07.013.
15. Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB; Valve Academic Research Consortium (VARC)-2. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2). *Eur J Cardiothorac Surg*. 2012;42:S45–S60. doi: 10.1093/ejcts/ezs533.
16. Dvir D, Webb J, Brecker S, Bleiziffer S, Hildick-Smith D, Colombo A, Descoutures F, Hengstenberg C, Moat NE, Bekeredjian R, Napodano M, Testa L, Lefevre T, Guetta V, Nissen H, Hernández JM, Roy D, Teles RC, Segev A, Dumonteil N, Fiorina C, Gotzmann M, Tchetche D, Abdel-Wahab M, De Marco F, Baumbach A, Laborde JC, Kornowski R. Transcatheter aortic valve replacement for degenerative bioprosthetic surgical valves: results from the global valve-in-valve registry. *Circulation*. 2012;126:2335–2344. doi: 10.1161/CIRCULATIONAHA.112.104505.
17. Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, Fontana GP, Dewey TM, Thourani VH, Pichard AD, Fischbein M, Szeto WY, Lim S, Greason KL, Teirstein PS, Malaisrie SC, Douglas PS, Hahn RT, Whisenant B, Zajarias A, Wang D, Akin JJ, Anderson WN, Leon MB; PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med*. 2012;366:1686–1695. doi: 10.1056/NEJMoa1200384.
18. van der Straaten EP, Rademakers LM, van Straten AH, Houterman S, Tan ME, Soliman Hamad MA. Mid-term haemodynamic and clinical results after aortic valve replacement using the Freedom Solo stentless bioprosthesis versus the Carpentier Edwards Perimount stented bioprosthesis. *Eur J Cardiothorac Surg*. 2016;49:1174–1180. doi: 10.1093/ejcts/ezv255.
19. Dellgren G, David TE, Raanani E, Armstrong S, Ivanov J, Rakowski H. Late hemodynamic and clinical outcomes of aortic valve replacement with the Carpentier-Edwards Perimount pericardial bioprosthesis. *J Thorac Cardiovasc Surg*. 2002;124:146–154.
20. Head SJ, Mokhles MM, Osnabrugge RL, Pibarot P, Mack MJ, Takkenberg JJ, Bogers AJ, Kappetein AP. The impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement: a systematic review and meta-analysis of 34 observational studies comprising 27 186 patients with 133 141 patient-years. *Eur Heart J*. 2012;33:1518–1529. doi: 10.1093/eurheartj/ehs003.
21. Astudillo LM, Santana O, Urbandt PA, Benjo AM, Elkayam LU, Nascimento FO, Lamas GA, Lamelas J. Clinical predictors of prosthesis-patient mismatch after aortic valve replacement for aortic stenosis. *Clinics (Sao Paulo)*. 2012;67:55–60.

22. Hernandez-Vaquero D, Garcia JM, Diaz R, Calvo D, Khalpey Z, Hernández E, Rodriguez V, Morís C, Llosa JC. Moderate patient-prosthesis mismatch predicts cardiac events and advanced functional class in young and middle-aged patients undergoing surgery due to severe aortic stenosis. *J Card Surg*. 2014;29:127–133. doi: 10.1111/jocs.12265.
23. Flameng W, Rega F, Vercalsteren M, Herijgers P, Meuris B. Antimineralization treatment and patient-prosthesis mismatch are major determinants of the onset and incidence of structural valve degeneration in bioprosthetic heart valves. *J Thorac Cardiovasc Surg*. 2014;147:1219–1224. doi: 10.1016/j.jtcvs.2013.03.025.
24. Nielsen-Kudsk JE, Christiansen EH, Terkelsen CJ, Nørgaard BL, Jensen KT, Krusell LR, Tang M, Terp K, Klaaborg KE, Andersen HR. Fracturing the ring of small mitroflow bioprostheses by high-pressure balloon predilatation in transcatheter aortic valve-in-valve implantation. *Circ Cardiovasc Interv*. 2015;8:e002667. doi: 10.1161/CIRCINTERVENTIONS.115.002667.
25. Tanase D, Grohmann J, Schubert S, Uhlemann F, Eicken A, Ewert P. Cracking the ring of Edwards Perimount bioprosthesis with ultrahigh pressure balloons prior to transcatheter valve in valve implantation. *Int J Cardiol*. 2014;176:1048–1049. doi: 10.1016/j.ijcard.2014.07.175.
26. Zenses AS, Mitchell J, Evin M, Stanova V, Obadia JF, Pibarot P, Rieu R. In vitro study of valve-in-valve performance with the CoreValve self-expandable prosthesis implanted in different positions and sizes within the Trifecta surgical heart valve. *Comput Methods Biomech Biomed Engin*. 2015;18(suppl 1):2086–2087. doi: 10.1080/10255842.2015.1069634.
27. Sedaghat A, Sinning JM, Utzenrath M, Ghalati PF, Schmitz C, Werner N, Nickenig G, Grube E, Ensminger S, Steinseifer U, Kuetting M. Hydrodynamic performance of the Medtronic CoreValve and the Edwards Sapien XT transcatheter heart valve in surgical bioprostheses: an in vitro valve-in-valve model. *Ann Thorac Surg*. 2016;101:118–124. doi: 10.1016/j.athoracsur.2015.06.047.

Circulation
Cardiovascular Interventions

Transcatheter Replacement of Failed Bioprosthetic Valves: Large Multicenter Assessment of the Effect of Implantation Depth on Hemodynamics After Aortic Valve-in-Valve

Matheus Simonato, John Webb, Ran Kornowski, Alec Vahanian, Christian Frerker, Henrik Nissen, Sabine Bleiziffer, Alison Duncan, Josep Rodés-Cabau, Guilherme F. Attizzani, Eric Horlick, Azeem Latib, Raffi Bekeredjian, Marco Barbanti, Thierry Lefevre, Alfredo Cerillo, José María Hernández, Giuseppe Bruschi, Konstantinos Spargias, Alessandro Iadanza, Stephen Brecker, José Honório Palma, Ariel Finkelstein, Mohamed Abdel-Wahab, Pedro Lemos, Anna Sonia Petronio, Didier Champagnac, Jan-Malte Sinning, Stefano Salizzoni, Massimo Napodano, Claudia Fiorina, Antonio Marzocchi, Martin Leon and Danny Dvir

Circ Cardiovasc Interv. 2016;9:
doi: 10.1161/CIRCINTERVENTIONS.115.003651
Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-7640. Online ISSN: 1941-7632