

SUPPLEMENTAL INFORMATION

HEART VALVE SIZING AND CLINICAL OUTCOMES IN PATIENTS UNDERGOING TRANSCATHETER AORTIC VALVE REPLACEMENT

Okuno et al.

Corresponding Author:

Stefan Stortecky, MD
Associate Professor of Cardiology
Department of Cardiology
Inselspital, Bern University Hospital
University of Bern
3010 Bern, Switzerland
Phone: 0041 31 632 83 52
Fax: 0041 31 634 10 69
Mail: Stefan.Stortecky@insel.ch

TABLE OF CONTENTS

ADDITIONAL METHODS. Data collection and clinical endpoints..... 3

SUPPLEMENTAL FIGURE. Annulus dimension and sizing according to the recommendation of the manufacturers..... 4

SUPPLEMENTAL TABLE 1. Sizing algorithm for each transcatheter heart valves (THV). 5

SUPPLEMENTAL TABLE 2. MDCT and Procedural characteristics according to Over-/Under-sized THV..... 10

SUPPLEMENTAL TABLE 3. Procedural complications and outcomes according to Over-/Under-sized THV 11

SUPPLEMENTAL TABLE 4. 30-days and 1-year clinical outcomes according Over-/Under-sized THV..... 12

ADDITIONAL REFERENCES..... 13

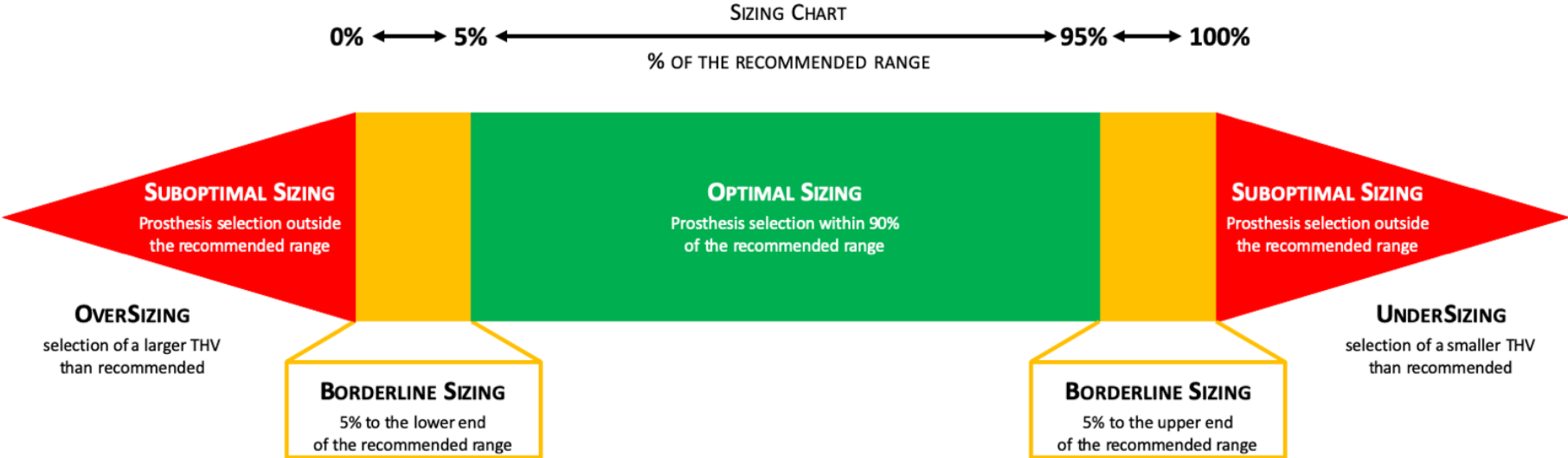
ADDITIONAL METHODS. Data collection and clinical endpoints.

Baseline clinical, procedural, and follow-up data were entered into a dedicated web-based database, held and maintained at the Clinical Trials Unit at the University of Bern, Bern, Switzerland. Follow-up data was obtained by standardized interviews, documentation from referring physicians, and hospital discharge summaries at 30 days and 1 year. All adverse events were systematically collected and adjudicated by a dedicated clinical event committee according to the Valve Academic Research Consortium (VARC-2) criteria.(1) VARC-2 device success was defined as the absence of procedural mortality and correct positioning of a single prosthetic heart valve into the proper anatomical location and intended performance. Given the high prevalence of prosthesis-patient mismatch,(2) modified device success defined as VARC-2 device success excluding prosthesis-patient mismatch was also assessed in the present analysis. VARC-2 early safety endpoint included a combination of all-cause mortality, stroke, life-threatening bleeding, acute kidney injury stage 2 or 3, coronary artery obstruction requiring intervention, major vascular complication, and valve-related dysfunction requiring repeat procedure at 30 days. The VARC-2 time-related valve safety endpoint included valve dysfunction, endocarditis, thrombotic complications of the prosthesis, and bleeding events up to 1 year. Unplanned repeat intervention was defined as a composite endpoint including repeat TAVI, repeat balloon valvuloplasty in another setting, surgical revision, or paravalvular leak closure for the implanted THV. The primary endpoint of the present analysis was a composite of all-cause death or unplanned repeat intervention at 1 year after TAVI.

SUPPLEMENTAL FIGURE. Annulus dimension and sizing according to the recommendation of the manufacturers.

ANNULUS DIMENSION AND SIZING ACCORDING TO THE RECOMMENDATION OF THE MANUFACTURERS

PERIMETER FOR SELF-EXPANDING DEVICES
AREA FOR BALLOON-EXPANDABLE DEVICES



SUPPLEMENTAL TABLE 1. Sizing algorithm for each transcatheter heart valves (THV).

Patients treated with SAPIEN THV/XT				
Implanted size	20mm	23mm	26mm	29mm
Annulus size recommendation		Area 314-415 (101) mm ³	Area 415-530 (115) mm ³	Area 530-660 (130) mm ³
Optimal sizing		319mm ³ <Area<410mm ³	421mm ³ <Area<524mm ³	537mm ³ <Area<653mm ³
Borderline sizing		Area 314-319mm ³ Area 410-415mm ³	Area 415-421mm ³ Area 524-530mm ³	Area 530-537mm ³ Area 653-660mm ³
Suboptimal sizing		Area <314mm ³ Area >415mm ³	Area <415mm ³ Area >530mm ³	Area <530mm ³ Area >660mm ³
Oversizing		Area <319mm ³	Area <421mm ³	Area <537mm ³
Undersizing		Area >410mm ³	Area >524mm ³	Area >653mm ³
Patients treated with SAPIEN 3				
Implanted size	20mm	23mm	26mm	29mm

Annulus size recommendation		Area 338-430 (93) mm ³	Area 430-546 (116) mm ³	Area 540-683 (143) mm ³
Optimal sizing		343mm ³ <Area<425mm ³	436mm ³ <Area<540mm ³	547mm ³ <Area<676mm ³
Borderline sizing		Area 338-343mm ³ Area 425-430mm ³	Area 430-436mm ³ Area 540-546mm ³	Area 540-547mm ³ Area 676-683mm ³
Suboptimal sizing		Area <338mm ³ Area >430mm ³	Area <430mm ³ Area >546mm ³	Area <540mm ³ Area >683mm ³
Oversizing		Area <343mm ³	Area <436mm ³	Area <547mm ³
Undersizing		Area >425mm ³	Area >540mm ³	Area >676mm ³
Patients treated with CoreValve*				
Implanted size	23mm	26mm	29mm	31mm
Annulus size recommendation	Perimeter 56.5-62.8 (6.3) mm	Perimeter 62.8-72.3 (9.5) mm	Perimeter 72.3-84.8 (12.5) mm	Perimeter 81.6-91.1 (9.5) mm
Optimal sizing	56.8mm<Perimeter<62.5mm	63.3mm<Perimeter<71.8mm	72.9mm<Perimeter<84.2mm	82.1mm<Perimeter<90.6mm
Borderline sizing	Perimeter 56.5-56.8mm Perimeter 62.5-62.8mm	Perimeter 62.8-63.3mm Perimeter 71.8-72.3mm	Perimeter 72.3-72.9mm Perimeter 84.2-84.8mm	Perimeter 81.6-82.1mm Perimeter 90.6-91.1mm
Suboptimal sizing	Perimeter <56.5mm Perimeter >62.8mm	Perimeter <62.8mm Perimeter >72.3mm	Perimeter <72.3mm Perimeter >84.8mm	Perimeter <81.6mm Perimeter >91.1mm

Oversizing	Perimeter <56.8mm	Perimeter <63.3mm	Perimeter <72.9mm	Perimeter <82.1mm
Undersizing	Perimeter >62.5mm	Perimeter >71.8mm	Perimeter >84.2mm	Perimeter >90.6mm
Evolut R/PRO				
Implanted size	23mm	26mm	29mm	34mm
Annulus size recommendation	Perimeter 56.5-62.8 (6.3) mm	Perimeter 62.8-72.3 (9.5) mm	Perimeter 72.3-81.7 (9.4) mm	Perimeter 81.7-94.2 (12.5) mm
Optimal sizing	56.8mm<Perimeter<62.5mm	63.3mm<Perimeter<71.8mm	72.8mm<Perimeter<81.2mm	82.3mm<Perimeter<93.6mm
Borderline sizing	Perimeter 56.5-56.8mm Perimeter 62.5-62.8mm	Perimeter 62.8-63.3mm Perimeter 71.8-72.3mm	Perimeter 72.3-72.8mm Perimeter 81.2-81.7mm	Perimeter 81.7-82.3mm Perimeter 93.6-94.2mm
Suboptimal sizing	Perimeter <56.5 Perimeter >62.8mm	Perimeter <62.8 Perimeter >72.3mm	Perimeter <72.3mm Perimeter >81.7mm	Perimeter <81.7mm Perimeter >94.2mm
Oversizing	Perimeter <56.8mm	Perimeter <63.3mm	Perimeter <72.8mm	Perimeter <82.3mm
Undersizing	Perimeter >62.5mm	Perimeter >71.8mm	Perimeter >81.2mm	Perimeter >93.6mm
SJM Portico				
Implanted size	23mm	25mm	27mm	29mm

Annulus size recommendation	Perimeter 60-66 (6) mm	Perimeter 66-73 (7) mm	Perimeter 72-79 (7) mm	Perimeter 79-85 (6) mm
Optimal sizing	60.3mm<Perimeter<65.7mm	66.4mm<Perimeter<72.6mm	72.4mm<Perimeter<78.6mm	79.3mm<Perimeter<84.7mm
Borderline sizing	Perimeter 60-60.3mm Perimeter 65.7-66mm	Perimeter 66-66.4mm Perimeter 72.6-73mm	Perimeter 72-72.4mm Perimeter 78.6-79mm	Perimeter 79-79.3mm Perimeter 84.7-85mm
Suboptimal sizing	Perimeter <60mm Perimeter >66mm	Perimeter <66mm Perimeter >73mm	Perimeter <72mm Perimeter >79mm	Perimeter <79mm Perimeter >85mm
Oversizing	Perimeter <60.3mm	Perimeter <66.4mm	Perimeter <72.4mm	Perimeter <79.3mm
Undersizing	Perimeter >65.7mm	Perimeter >72.6mm	Perimeter >78.6mm	Perimeter >84.7mm
Symetis Acurate/Acurate neo				
Implanted size	S	M	L	
Annulus size recommendation	Perimeter 66-72 (6) mm	Perimeter 72-79 (7) mm	Perimeter 79-85 (6) mm	
Optimal sizing	66.3mm<Perimeter<71.7mm	72.4mm<Perimeter<78.6mm	79.3mm<Perimeter<84.7mm	
Borderline sizing	Perimeter 66-66.3mm Perimeter 71.7-72mm	Perimeter 72-72.4mm Perimeter 78.6-79mm	Perimeter 79-79.3mm Perimeter 84.7-85mm	
Suboptimal sizing	Perimeter <66mm Perimeter >72mm	Perimeter <72mm Perimeter >79mm	Perimeter <79mm Perimeter >85mm	

Oversizing	Perimeter <66.3mm	Perimeter <72.4mm	Perimeter <79.3mm
Undersizing	Perimeter >71.7mm	Perimeter >78.6mm	Perimeter >84.7mm
Lotus/Lotus edge			
Implanted size	23mm	25mm	27mm
Annulus size recommendation	Perimeter 62.8-72.3 (9.5) mm	Perimeter 72.3-78.5 (6.2) mm	Perimeter 78.5-84.8 (6.3) mm
Optimal sizing	63.3mm<Perimeter<71.8mm	72.6mm<Perimeter<78.2mm	78.8mm<Perimeter<84.5mm
Borderline sizing	Perimeter 62.8-63.3mm Perimeter 71.8-72.3mm	Perimeter 72.3-72.6mm Perimeter 78.2-78.5mm	Perimeter 78.5-78.8mm Perimeter 84.5-84.8mm
Suboptimal sizing	Perimeter <62.8mm Perimeter >72.3mm	Perimeter <72.3mm Perimeter >78.5mm	Perimeter <78.5mm Perimeter >84.8mm
Oversizing	Perimeter <63.3mm	Perimeter <72.6mm	Perimeter <78.8mm
Undersizing	Perimeter >71.8mm	Perimeter >78.2mm	Perimeter >84.5mm
*Manufacturer only provided annulus diameter for the recommendation. The recommended perimeter is derived from Eur Heat J 2014:35:2627-2638.			

SUPPLEMENTAL TABLE 2. MDCT and Procedural characteristics according to Over-/Under-sized THV

	OVERSIZING (N=212)	UNDERSIZING (N=198)	P-VALUE
COMPUTED TOMOGRAPHY DATA			
Bicuspid valve (n, %)	12 (5.7%)	19 (9.6%)	0.14
Annulus area (mm ²)	425.9±68.2	500.8±108.5	<0.001
Annulus perimeter (mm)	74.5±6.0	80.6±8.5	<0.001
SOV diameter (mm)	31.7±3.7	34.1±4.3	<0.001
AVC calcium (mm ³)	283.0±322.1	453.5±514.5	<0.001
LVOT calcium (mm ³)	15.2±49.8	25.5±60.2	0.058
Eccentricity of annulus (0 to 1)	0.76±0.06	0.76±0.06	0.89
PROCEDURAL CHARACTERISTICS			
Fluoroscopy time (min)	15.1±7.8	20.5±18.1	<0.001
General anesthesia (n, %)	47 (22.2%)	44 (22.2%)	1.00
Conversion from Local to General anesthesia (n, %)	6 (3.8%)	1 (0.8%)	0.14
Femoral main access site (n, %)	188 (88.7%)	178 (89.9%)	0.75
Type of valve (n, %)			<0.001
Balloon-expandable*	155 (73.1%)	44 (22.2%)	
Self-expanding**	52 (24.5%)	128 (64.6%)	
Mechanical-expanding***	5 (2.4%)	26 (13.1%)	
Valve size (n, %)			0.345
≤26mm	137 (64.6%)	119 (60.1%)	
>26mm	75 (35.4%)	79 (39.9%)	
Pre dilation (n, %)	143 (67.5%)	160 (80.8%)	0.002
Post dilation (n, %)	39 (18.4%)	92 (46.5%)	<0.001
Depicted are means with standard deviations (±SD) or counts with percentages (%). * SAPIEN THV/XT, SAPIEN; ** CoreValve, Evolut R/ PRO, Portico, Symetis ACURATE/ACURATE neo; *** Lotus/ Lotus Edge STS PROM = Society of Thoracic Surgeons Predicted Risk Of Mortality; NYHA = New York Heart Association; CKD = Chronic kidney disease; GFR = Glomerular filtration rate; COPD = Chronic obstructive pulmonary disease; LVEF = Left ventricular ejection fraction; AR = Aortic regurgitation; MR = Mitral regurgitation; TR = Tricuspid regurgitation; AVC = Aortic valvular complex; LVOT = Left ventricular outflow tract.			

SUPPLEMENTAL TABLE 3. Procedural complications and outcomes according to Over-/Under-sized THV

	OPTIMAL SIZING (N=1228)	OVERSIZING (N=212)	UNDERSIZING (N=198)	CRUDE RISK RATIO			
	A	B	C	B vs A		C vs A	
				RR (95% CI)	P-VALUE	RR (95% CI)	P-VALUE
PROCEDURAL COMPLICATIONS							
Valve in series (n, %)	17 (1.4)	3 (1.4)	7 (3.5)	1.02 (0.30-3.46)	0.97	2.55 (1.07-6.08)	0.034
Valve migration/embolization (n, %)	21 (1.7)	3 (1.4)	8 (4.0)	0.83 (0.25-2.75)	0.76	2.36 (1.06-5.26)	0.035
Annulus rupture/aortic dissection (n, %)	6 (0.5)	3 (1.4)	1 (0.5)	2.90 (0.73-11.50)	0.13	1.03 (0.13-8.55)	0.98
Cardiac tamponade/rupture (n, %)	10 (0.8)	4 (1.9)	0 (0.0)	2.32 (0.73-7.32)	0.15	0.29 (0.02-4.93)	0.37
Coronary artery occlusion (n, %)	5 (0.4)	1 (0.5)	0 (0.0)	1.16 (0.14-9.87)	0.89	0.56 (0.03-10.09)	1.0
Conversion to Surgery (n, %)	10 (0.8)	1 (0.5)	0 (0.0)	0.58 (0.07-4.50)	0.60	0.29 (0.02-4.93)	0.37
PROCEDURAL OUTCOMES							
VARC-2 device success (n, %)	555 (57.8%)	89 (54.3%)	77 (47.8%)	0.94 (0.81-1.09)	0.41	0.83 (0.70-0.98)	0.029
Modified device Success (n, %)*	1035 (87.4)	191 (91.8)	154 (79.0)	1.05 (1.00-1.10)	0.036	0.90 (0.84-0.97)	0.008
Mean prosthetic gradient > 20mmHg (n, %)	25 (2.0)	6 (2.8)	2 (1.0)	1.38 (0.57-3.33)	0.47	0.50 (0.12-2.08)	0.34
Prosthesis-patient mismatch (n, %)	309 (33.5)	61 (38.6)	50 (34.7)	1.15 (0.93-1.43)	0.20	1.04 (0.81-1.32)	0.77
Moderate or severe AR (n, %)**	77 (7.2)	5 (2.4)	28 (14.2)	0.33 (0.14-0.80)	0.014	1.98 (1.33-2.95)	0.001
Procedural, discharge and post-procedure outcomes analyzed with robustified binomial generalized linear models using a log-link and risk ratios RR (95% confidence interval CI) are reported.							
*Device success is defined as VARC-2 device success excluding prosthesis patient mismatch.							
VARC = Valve Academic Research Consortium; AR = Aortic regurgitation.							

SUPPLEMENTAL TABLE 4. 30-days and 1-year clinical outcomes according Over-/Under-sized THV

	OPTIMAL SIZING (N=1228)	OVER- SIZING (N=212)	UNDER- SIZING (N=198)	CRUDE HAZARD RATIO				ADJUSTED HAZARD RATIO			
	A	B	C	B vs A		C vs A		B vs A		C vs A	
				HR (95% CI)	P-value	HR (95% CI)	P-value	HR _{adj} (95% CI)	P-value	HR _{adj} (95% CI)	P-value
At 30 days											
VARC-2 Early safety (n, %)	223 (18.2)	42 (19.8)	45 (22.7)	1.10 (0.79-1.53)	0.58	1.27 (0.92-1.74)	0.15	1.17 (0.84-1.63)	0.35	1.26 (0.92-1.74)	0.15
All-cause mortality (n, %)	29 (2.4)	9 (4.3)	11 (5.6)	1.82 (0.86-3.84)	0.12	2.37 (1.18-4.75)	0.015	2.05 (0.96-4.36)	0.063	2.25 (1.12-4.51)	0.023
All stroke (disabling and nondisabling) (n, %)	37 (3.0)	6 (2.9)	11 (5.6)	0.94 (0.40-2.23)	0.89	1.88 (0.96-3.69)	0.065	0.95 (0.40-2.25)	0.90	1.90 (0.96-3.74)	0.064
Life-threatening bleeding (n, %)	80 (6.5)	15 (7.1)	16 (8.1)	1.09 (0.63-1.89)	0.76	1.24 (0.73-2.13)	0.43	1.20 (0.69-2.10)	0.51	1.29 (0.75-2.21)	0.36
Major vascular complication (n, %)	131 (10.7)	28 (13.2)	15 (7.6)	1.24 (0.83-1.87)	0.30	0.71 (0.41-1.20)	0.20	1.31 (0.87-1.97)	0.20	0.70 (0.41-1.19)	0.19
Acute kidney injury stage 2 or 3 (n, %)	246 (20.2)	34 (16.3)	45 (23.1)	0.54 (0.17-1.78)	0.31	1.37 (0.60-3.10)	0.45	0.67 (0.20-2.22)	0.52	1.52 (0.67-3.48)	0.32
Permanent pacemaker implantation (n, %)	223 (18.2)	42 (19.8)	45 (22.7)	0.78 (0.54-1.12)	0.17	1.15 (0.84-1.58)	0.39	0.78 (0.55-1.12)	0.19	1.09 (0.79-1.50)	0.60
1 year											
Composite of all-cause death or unplanned repeat intervention (n, %)	149 (12.3)	23 (10.9)	44 (22.2)	0.90 (0.58-1.39)	0.622	1.92 (1.37-2.69)	<0.001	0.94 (0.61-1.46)	0.79	1.86 (1.32-2.60)	<0.001
VARC-2 Time-related valve safety (n, %)	488 (40.5)	65 (31.7)	90 (46.3)	0.72 (0.55-0.93)	0.012	1.25 (1.00-1.57)	0.051	0.73 (0.56-0.94)	0.017	1.23 (0.99-1.55)	0.067
All-cause mortality (n, %)	142 (11.7)	22 (10.5)	41 (20.7)	0.90 (0.57-1.41)	0.644	1.87 (1.32-2.65)	<0.001	0.95 (0.61-1.50)	0.834	1.80 (1.27-2.55)	0.001
Cardiovascular mortality (n, %)	94 (7.9)	14 (6.8)	29 (15.1)	0.86 (0.49-1.52)	0.612	1.99 (1.31-3.02)	0.001	0.93 (0.53-1.64)	0.811	1.94 (1.28-2.95)	0.002
Unplanned repeat intervention (n, %)	10 (0.8)	1 (0.5)	5 (2.7)	0.58 (0.07-4.56)	0.607	3.17 (1.08-9.27)	0.035	0.54 (0.07-4.24)	0.559	3.35 (1.13-9.91)	0.029
Outcomes analyzed with Cox's regressions with hazard ratios (HR 95% CI) reported, censoring patients at last valid contact or death; adjusting for age, gender, BMI >30 kg/m ² , LVEF <40%, STS PROM, access site.											

ADDITIONAL REFERENCES

1. Kappetein AP, Head SJ, Genereux P et al. 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:S45-60.
2. Okuno T, Khan F, Asami M et al. Prosthesis-Patient Mismatch Following Transcatheter Aortic Valve Replacement With Supra-Annular and Intra-Annular Prostheses. *JACC Cardiovasc Interv* 2019.