

SUPPLEMENTARY DATA

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Table S1. Enrolling centers

Center	Enrolled patients
Kerkhoff-Klinik, Bad Nauheim, Germany	244
The Heart Center, Rigshospitalet, Copenhagen University Hospital, Denmark	160
A.O.U. Policlinico "G. Rodolico-San Marco", Catania, Italy	88
Clinique Pasteur, Toulouse, France	57
Fondazione Policlinico Universitario A. Gemelli, Rome, Italy	53
Cedars-Sinai Heart Institute, Los Angeles, CA, USA	41
Leeds Teaching Hospitals NHS Trust, Leeds, UK	40
Galway University Hospitals, Ireland	33
Ospedale San Raffaele, Milano, Italy	30
Università di Padova, Padova, Italy	27
ASST Spedali Civili di Brescia, University of Brescia, Italy	22
Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA	21
West China Hospital, Sichuan University, China	20
IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy	18
University Clinical Hospital of Valladolid, Valladolid, Spain	17
Fondazione Poliambulanza Istituto Ospedaliero, Brescia, Italy	14
Ca' Foncello Hospital, Treviso, Italy	15
IRCCS Policlinico San Donato, San Donato Milanese, Milano, Italy	13
Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy	12
IRCCS Humanitas Research Hospital, Rozzano-Milano, Italy	12
German Heart Centre Munich, München, Germany	10
Edith Wolfson Medical Center, Holon, Israel	5
IRCCS Ospedale Galeazzi-Sant'Ambrogio, Milano, Italy	3
Clinica Mediterranea, Napoli, Italy	1

Table S2. Current recommendations for grading the severity of native aortic regurgitation according to the main qualitative, semi-quantitative and quantitative parameters

Aortic leaflets	Abnormal/flail, or wide coaptation defect
LV size	Usually dilated
Diastolic flow reversal in descending aorta (PW)	Prominent holodiastolic reversal with EDV ≥ 20 cm/s
Jet width/LVOT width, central jets (%)	≥ 65
VC width (cm)	> 0.6
PHT (msec)	< 200
RVol (mL/beat)	≥ 60
RF (%)	≥ 50
EROA (cm ²)	≥ 0.30

Abbreviations: EDV=end-diastolic volume; EROA=effective regurgitation orifice area; LV=left ventricle; LVOT=left ventricle outflow tract; PHT=pressure half-time; PW=pulsed wave; RF=regurgitant fraction; RVol=regurgitant volume; VC=vena contracta.

Table S3. Current recommendations for grading the severity of post-TAVI aortic regurgitation according to the main qualitative, semi-quantitative and quantitative parameters

Position of prosthesis	Frequently abnormal
Stent and leaflet morphology	Frequently abnormal
Diastolic flow reversal in descending aorta (PW)	Prominent holodiastolic reversal with EDV ≥ 20 cm/s
Circumferential extent of PVR (%)	≥ 30
VC width (cm)	> 0.6
PHT (msec)	< 200
RVol (mL/beat)	≥ 60
RF (%)	≥ 50
EROA (cm ²)	≥ 0.30

Abbreviations: EDV=end-diastolic volume; EROA=effective regurgitation orifice area; PHT=pressure half-time; PVR=paravalvular regurgitation; PW=pulsed wave; RF=regurgitant fraction; RVol=regurgitant volume; VC=vena contracta.

Table S4. Clusters and sizes of transcatheter heart valves

	Total (n = 956)	Mixed BAV disease (n = 134)	Pure BAV stenosis (n = 956)
Sapien 3/3 Ultra	409 (42.8)	53 (39.2)	356 (43.3)
20 mm	1	0	1
23 mm	67	6	61
26 mm	181	22	159
29 mm	160	25	135
Evolut R	164 (17.2)	29 (21.6)	135 (16.4)
23 mm	7	0	7
26 mm	25	7	18
29 mm	35	6	29
34 mm	97	16	81
Evolut Pro/Pro +	216 (22.6)	29 (21.7)	187 (22.7)
23 mm	1	1	0
26 mm	49	4	45
29 mm	134	18	116
34 mm	32	6	26
Acurate Neo	52 (5.4)	7 (5.2)	45 (5.5)
23 mm	12	3	9
25 mm	17	0	17
27 mm	23	4	19
Acurate Neo2	38 (4.0)	2 (1.5)	36 (4.4)
23 mm	13	1	12
25 mm	12	0	12
27 mm	13	1	12
Portico	39 (4.1)	5 (3.7)	34 (4.1)
23 mm	3	2	1
25 mm	3	0	3
27 mm	10	0	10
29 mm	23	3	20
Navitor	14 (1.5)	1 (0.7)	13 (1.6)
25 mm	4	0	4
27 mm	6	0	6
29 mm	4	1	3

Venus A plus	10 (1.1)	3 (2.2)	7 (0.9)
23 mm	1	0	1
26 mm	4	2	2
29 mm	5	1	4
Myval	7 (0.7)	1 (0.7)	6 (0.7)
24.5 mm	1	0	1
26 mm	3	0	3
27.5 mm	1	0	1
29 mm	1	1	0
30.5 mm	1	0	1
Prizvalve	5 (0.5)	3 (2.2)	2 (0.2)
23 mm	1	1	0
26 mm	1	0	1
29 mm	3	2	1
Taurus Valve	2 (0.2)	1 (0.7)	1 (0.1)
29 mm	2	1	1

Table S5. Two-sided test of the scaled Schoenfeld residuals over time

Outcome	Chi²	df	P value
Major adverse events	19.16	17	0.319
All-cause death	10.92	17	0.861
Cerebrovascular events	18.18	17	0.378
Hospitalization for heart failure	22.36	16	0.132
Cardiovascular death	13.54	17	0.6994

Table S6. Subgroup analysis according to post-TAVR AR

Outcome	Post-TAVR No/Mild AR				Post-TAVR Moderate/Severe AR				P for interaction
	Mixed BAV disease (n=125)	Pure BAV stenosis (n=787)	HR _{adj} (95% CI)	P Value	Mixed BAV disease (n=8)	Pure BAV stenosis (n=28)	HR _{adj} (95% CI)	P Value	
MAE	11 (8.8)	127 (16.1)	0.49 (0.26-0.92)	0.026	0 (0.0)	11 (39.3)	-	-	-
All-cause death	7 (5.6)	87 (11.1)	0.44 (0.20-0.97)	0.041	0 (0.0)	6 (21.4)	-	-	-
Cerebrovascular events	4 (3.2)	39 (5.0)	0.67 (0.24-1.93)	0.463	0 (0.0)	2 (7.1)	-	-	-
Hospitalization for heart failure	1 (0.8)	18 (2.3)	0.26 (0.03-2.06)	0.201	0 (0.0)	4 (14.3)	-	-	-
Cardiovascular death	1 (0.8)	37 (4.7)	0.12 (0.02-0.91)	0.041	0 (0.0)	2 (7.1)	-	-	-

Adjusted for age, BSA, male sex, CAD, PAD, NYHA class, STS-PROM score, LVEF, eGFR, severe raphe calcification, severe annulus/LVOT calcification, pre-procedural MR grade.

Abbreviations: AR=aortic regurgitation; BSA=body surface area; CAD=coronary artery disease; CI=confidence interval; eGFR=estimated glomerular filtration rate; HR_{adj}=adjusted hazard ratio; LVEF=left ventricular ejection fraction; LVOT=left ventricular outflow tract; MAE=major adverse events; MR=mitral regurgitation; NYHA=New York Heart Association; PAD=peripheral arterial disease; STS-PROM=Society of Thoracic Surgeons-Predicted Risk Of Mortality.

Table S7. Subgroup analysis according to raphe calcification

Outcome	Severe raphe calcification (n=254)				Non-severe raphe calcification (n=702)				P for interaction
	Mixed BAV disease (n=43)	Pure BAV stenosis (n=211)	HR _{adj} (95% CI)	P Value	Mixed BAV disease (n=91)	Pure BAV stenosis (n=611)	HR _{adj} (95% CI)	P Value	
MAE	6 (14.0)	36 (17.1)	0.78 (0.30-2.03)	0.612	6 (6.69)	108 (17.7)	0.33 (0.14-0.77)	0.010	0.104
All-cause death	4 (9.3)	31 (14.7)	0.55 (0.17-1.72)	0.301	4 (4.4)	68 (11.1)	0.37 (0.13-1.03)	0.056	0.494
Cerebrovascular events	3 (7.0)	9 (4.3)	0.92 (0.16-5.20)	0.928	1 (1.1)	33 (5.4)	0.25 (0.03-1.83)	0.171	0.067
Hospitalization for heart failure	0 (0.0)	3 (1.4)	-	-	1 (1.1)	19 (3.1)	0.27 (0.03-2.14)	0.215	-
Cardiovascular death	1 (2.3)	16 (7.6)	0.17 (0.02-1.45)	0.105	1 (1.1)	29 (4.7)	0.21 (0.03-1.57)	0.127	0.873

Adjusted for age, BSA, male sex, CAD, PAD, NYHA class, STS-PROM score, LVEF, eGFR, severe raphe calcification, severe annulus/LVOT calcification, pre-procedural MR grade.

Abbreviations: AR=aortic regurgitation; BSA=body surface area; CAD=coronary artery disease; CI=confidence interval; eGFR=estimated glomerular filtration rate; HR_{adj}=adjusted hazard ratio; LVEF=left ventricular ejection fraction; LVOT=left ventricular outflow tract; MAE=major adverse events; MR=mitral regurgitation; NYHA=New York Heart Association; PAD=peripheral arterial disease; STS-PROM=Society of Thoracic Surgeons-Predicted Risk Of Mortality.

Table S8. Subgroup analysis according to raphe localization

Outcome	R-L (n=814)				L-R or L-NC (n=142)				P for interaction
	Mixed BAV disease (n=106)	Pure BAV stenosis (n=708)	HR _{adj} (95% CI)	P Value	Mixed BAV disease (n=114)	Pure BAV stenosis (n=28)	HR _{adj} (95% CI)	P Value	
MAE	11 (10.4)	129 (18.2)	0.53 (0.28-1.00)	0.054	1 (3.6)	15 (13.2)	0.34 (0.04-3.28)	0.354	0.488
All-cause death	7 (6.6)	88 (12.4)	0.47 (0.21-1.05)	0.067	1 (3.6)	11 (9.6)	0.34 (0.03-4.32)	0.406	0.494
Cerebrovascular events	4 (3.8)	38 (5.4)	0.78 (0.27-2.25)	0.647	0 (0.0)	4 (3.5)	-	-	-
Hospitalization for heart failure	1 (0.9)	21 (3.0)	0.28 (0.04-2.20)	0.225	0 (0.0)	1 (0.9)	-	-	-
Cardiovascular death	2 (1.9)	40 (5.6)	0.26 (0.06-1.11)	0.068	0 (0.0)	5 (4.4)	-	-	-

Adjusted for age, BSA, male sex, CAD, PAD, NYHA class, STS-PROM score, LVEF, eGFR, severe raphe calcification, severe annulus/LVOT calcification, pre-procedural MR grade.

Abbreviations: AR=aortic regurgitation; BSA=body surface area; CAD=coronary artery disease; CI=confidence interval; eGFR=estimated glomerular filtration rate; HR_{adj}=adjusted hazard ratio; LVEF=left ventricular ejection fraction; LVOT=left ventricular outflow tract; MAE=major adverse events; MR=mitral regurgitation; NYHA=New York Heart Association; PAD=peripheral arterial disease; STS-PROM=Society of Thoracic Surgeons-Predicted Risk Of Mortality.

Table S9. Sensitivity analysis stratified by baseline AR severity into three groups

Outcome	No AR (n=442)	Mild AR (n=380)	Moderate/Severe AR (n=134)	Mild AR vs. No AR		Moderate/Severe AR vs. No AR	
				HR _{adj} (95% CI)	P Value	HR _{adj} (95% CI)	P Value
MAE	73 (16.5)	71 (18.7)	12 (9.0)	0.96 (0.67-1.36)	0.803	0.46 (0.24-0.86)	0.015
All-cause death	54 (12.2)	45 (11.8)	8 (6.0)	0.81 (0.53-1.25)	0.335	0.39 (0.18-0.85)	0.018
Cerebrovascular events	22 (5.0)	20 (5.3)	4 (3.0)	0.84 (0.44-1.59)	0.583	0.55 (0.18-1.66)	0.290
Hospitalization for heart failure	11 (2.5)	11 (2.9)	1 (0.7)	1.02 (0.40-2.62)	0.966	0.25 (0.03-2.04)	0.194
Cardiovascular death	26 (5.9)	19 (5.0)	2 (1.5)	0.75 (0.39-1.44)	0.384	0.18 (0.04-0.81)	0.025

Adjusted for age, BSA, male sex, CAD, PAD, NYHA class, STS-PROM score, LVEF, eGFR, severe raphe calcification, severe annulus/LVOT calcification, pre-procedural MR grade.

Abbreviations: AR=aortic regurgitation; BSA=body surface area; CAD=coronary artery disease; CI=confidence interval; eGFR=estimated glomerular filtration rate; HR_{adj}=adjusted hazard ratio; LVEF=left ventricular ejection fraction; LVOT=left ventricular outflow tract; MAE=major adverse events; MR=mitral regurgitation; NYHA=New York Heart Association; PAD=peripheral arterial disease; STS-PROM=Society of Thoracic Surgeons-Predicted Risk Of Mortality.