

## Supplementary Online Content

Yang LT, Lee CC, Su CH, et al. Analysis of left ventricular indexes and mortality among Asian adults with hemodynamically significant chronic aortic regurgitation. *JAMA Netw Open*. 2023;6(3):e234632. doi:10.1001/jamanetworkopen.2023.4632

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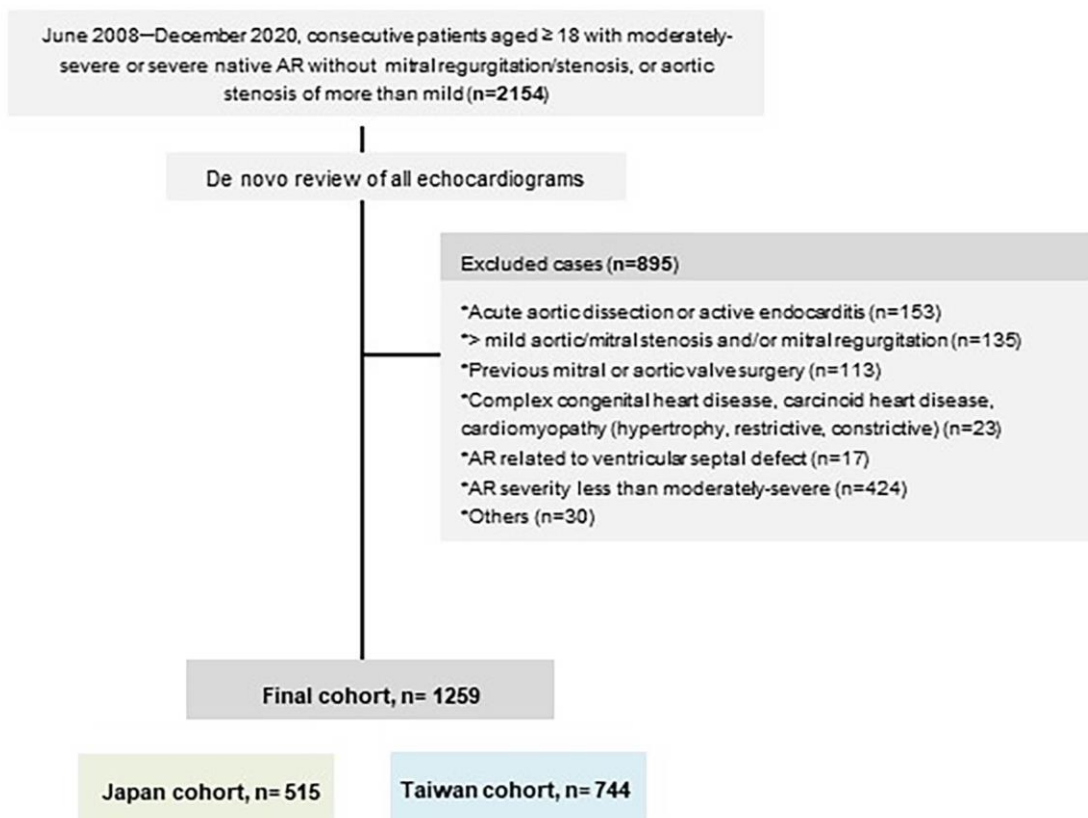
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This supplementary material has been provided by the authors to give readers additional information about their work.

**eFigure 1. Study Flow**



**eTable 1. Factors Linked to Aortic Valve Surgical Intervention in Taiwanese and Japanese Individuals**

	Taiwan (n=744, 258 AVS)		Japan (n=515, 225 AVS)	
	HR(95% CI)	P value	HR(95% CI)	P value
Model 1*				
<b>LVESDi, mm/m<sup>2</sup></b>	1.06(1.04-1.08)	<0.0001	1.05(1.02-1.07)	<0.0001
Model 2*				
<b>LVEF per 10%</b>	0.84(0.74-0.96)	0.01	0.84(0.73-0.96)	0.01
Model 3*				
<b>LVESVi per 10ml/m<sup>2</sup></b>	1.12(1.08-1.17)	<0.0001	1.10(1.05-1.15)	<0.0001

See abbreviations from Table 2 and Table 3.

\*All models were adjusted for age, sex, Charlson score, and New York Heart Association functional class.

**eTable 2.** Univariate Cox Proportional Hazards Regression Analysis for Factors Associated With All-cause Death Under Medical Surveillance (n=201).

	Total, n=1259		Taiwan, n=744		Japan, n=515	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Age	1.08(1.06-1.09)	< <b>0.0001</b>	1.07(1.06-1.09)	< <b>0.0001</b>	1.08(1.05-1.12)	< <b>0.0001</b>
Female	1.55(1.15-2.07)	<b>0.004</b>	1.77(1.27-2.46)	<b>0.001</b>	1.51(0.79-2.86)	0.21
CCI	1.42(1.34-1.50)	< <b>0.0001</b>	1.36(1.28-1.45)	< <b>0.0001</b>	1.62(1.43-1.83)	< <b>0.0001</b>
NYHA (I as reference)		< <b>0.0001</b>		< <b>0.0001</b>		<b>0.01</b>
II	2.04(1.48-2.81)		2.09(1.46-2.98)		1.44(0.68-3.08)	
III/IV	6.8(4.70-9.93)		7.45(4.90-11.3)		4.52(1.91-10.7)	
LVEF per 10%	0.70(0.62-0.80)	< <b>0.0001</b>	0.66(0.56-0.78)	< <b>0.0001</b>	0.59(0.46-0.75)	< <b>0.0001</b>
LVESDi, mm/m <sup>2</sup>	1.05(1.03-1.08)	< <b>0.0001</b>	1.08(1.05-1.11)	< <b>0.0001</b>	1.07(1.02-1.12)	<b>0.006</b>
LVESD, mm	1.00(0.98-1.02)	0.38	1.01(0.99-1.04)	0.08	1.01(0.97-1.05)	0.44
LVESDi <20 mm/m <sup>2</sup>	Reference		Reference		Reference	
20-25 mm/m <sup>2</sup>	1.31(0.90-1.92)	0.15	1.55(1.05-2.30)	<b>0.02</b>	1.01(0.22-4.63)	0.98
>25 mm/m <sup>2</sup>	2.04(1.38-3.01)	<b>0.0002</b>	3.00(1.96-4.59)	< <b>0.0001</b>	2.23(0.53-9.44)	0.27
LVESVi per 10ml/ m <sup>2</sup> *	1.06(1.00-1.12)	<b>0.02</b>	1.08(1.01-1.15)	<b>0.02</b>	1.14(1.05-1.24)	<b>0.006</b>
Taiwanese vs Japanese	1.99(1.39-2.84)	< <b>0.0001</b>				

CCI, Charlson comorbidity index. See Table 1 and 2 for abbreviations.

\*After adjusting for age, the hazard ratio, 95%, and p value for LVESVi per 10ml/m<sup>2</sup> in the total cohort, Taiwanese and Japanese was 1.07(1.02-1.12; P=0.005), 1.10(1.04-1.17; P=0.001), and 1.13(1.03-1.22; p=0.009).

†After adjustment for age, sex, Charlson score, and NYHA, the HR, CI, and P value of LVESD in the entire-, Taiwan-, Japan-cohort was 1.00(0.98-1.02), P=0.45 ; 1.02(1.00-1.04), P=0.035; 1.01(0.97-1.05), P=0.39, respectively.

**eTable 3.** Univariate Cox Proportional Hazards Regression Analysis for Factors Associated With All-cause Death During Total Follow-Up (n=240)

	Total, n=1259		Taiwan, n=744		Japan, n=515	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Age	1.07(1.06-1.09)	<0.0001	1.07(1.06-1.09)	<0.0001	1.08(1.05-1.11)	<0.0001
Female	1.54(1.17-2.02)	0.002	1.73(1.27-2.36)	0.0007	1.44(0.80-2.59)	0.22
CCI	1.47(1.39-1.54)	<0.0001	1.41(1.32-1.49)	<0.0001	1.63(1.45-1.83)	<0.0001
NYHA (I as reference)		<0.0001		<0.0001		0.001
II	1.85(1.38-2.48)		2.08(1.50-2.88)		1.00(0.50-2.01)	
III/IV	5.17(3.67-7.29)		5.31(3.58-7.88)		4.26(2.09-8.70)	
<b>Time-dependent AVS</b>	0.40(0.28-0.57)	<0.001	0.44(0.29-0.66)	<0.001	0.42(0.21-0.87)	0.01
LVEF per 10%	0.76(0.68-0.86)	<0.0001	0.70(0.61-0.81)	<0.0001	0.66(0.53-0.83)	0.0007
LVESDi, mm/m <sup>2</sup>	1.03(1.01-1.05)	0.003	1.06(1.03-1.08)	<0.0001	1.04(1.00-1.09)	0.03
LVESD, mm	0.99(0.97-1.00)	0.21	1.00(0.98-1.02)	0.85	0.99(0.96-1.02)	0.89
LVESDi <20 mm/m <sup>2</sup>	Reference		Reference		Reference	
20-25 mm/m <sup>2</sup>	1.26(0.87-1.82)	0.20	1.50(1.02-2.20)	0.03	1.08(0.24-4.81)	0.91
>25 mm/m <sup>2</sup>	1.64(1.14-2.37)	0.007	2.45(1.65-3.65)	<0.0001	1.82(0.43-7.61)	0.40
LVESVi per 10ml/ m <sup>2</sup> *	1.00(0.95-1.05)	0.81	1.02(1.08-0.97)	0.45	1.07(0.98-1.14)	0.08
Taiwanese vs Japanese	2.19(1.59-3.02)	<0.0001				

CCI, Charlson comorbidity index. See Table 1 for abbreviations.

\*After adjusting for age, the hazard ratio, 95%, and p value for LVESVi per 10ml/m<sup>2</sup> in the total cohort, Taiwanese and Japanese was 1.03(0.98-1.07; P=0.12), 1.05(1.00-1.10; P=0.042), and 1.11(1.01-1.19; p=0.017).

**eTable 4.** Multivariate Cox Proportional Hazards Regression Analysis for Factors Associated With Cardiovascular Death Under Medical Surveillance (n=74)\*

	Total, n=1259		Taiwan, n=744		Japan, n=515	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
<b>Model 1: LVEF</b>						
Age	1.05(1.03-1.07)	<0.0001	1.05(1.03-1.07)	<0.0001		
Female	1.81(1.11-2.95)	0.01	1.55(0.89-2.69)	0.12		
Charlson comorbidity index	1.09(0.96-1.24)	0.15	0.97(0.82-1.13)	0.78		
NYHA (I as reference)						
II	1.15(0.65-2.02)	0.61	1.28(0.69-2.37)	0.42		
III/IV	2.56(1.21-5.41)	0.01	3.95(1.72-9.03)	0.001		
LVEF per 10%	0.69(0.56-0.85)	0.0008	0.72(0.57-0.91)	0.007	0.47(0.32-0.70)	0.0006
Taiwanese vs Japanese	3.34(1.75-6.39)	<0.0001				
<b>Model 2: LVESDi</b>						
Age	1.05(1.03-1.07)	<0.0001	1.05(1.02-1.07)	<0.0001		
Female	1.60(0.98-2.60)	0.06	1.41(0.81-2.44)	0.22		
Charlson comorbidity index	1.13(0.99-1.28)	0.05	1.00(0.86-1.17)	0.90		
NYHA (I as reference)						
II	1.22(0.70-2.14)	0.46	1.35(0.73-2.49)	0.33		
III/IV	2.88(1.41-5.89)	0.003	4.12(1.86-9.12)	0.0005		
LVESDi, mm/m <sup>2</sup>	1.05(1.01-1.09)	0.01	1.05(1.00-1.10)	0.04	1.06(1.02-1.10)	0.0009
Taiwanese vs Japanese	3.33(1.70-6.49)	0.0001				
<b>Model 3: LVESVi</b>						
Age	1.05(1.03-1.08)	<0.0001	1.05(1.03-1.08)	<0.0001		
Female	2.00(1.21-3.29)	0.007	1.64(0.93-2.89)	0.08		
Charlson comorbidity index	1.13(1.00-1.28)	0.04	1.01(0.87-1.18)	0.80		
NYHA (I as reference)						
II	1.11(0.63-1.96)	0.69	1.25(0.67-2.34)	0.47		
III/IV	2.63(1.28-5.37)	0.007	4.04(1.81-8.99)	0.0006		
LVESVi per 10ml/m <sup>2</sup>	1.15(1.06-1.24)	0.0007	1.12(1.02-1.24)	0.02	1.10(1.02-1.18)	0.01
Taiwanese vs Japanese	3.69(1.89-7.22)	<0.0001				

See Table 1 for abbreviations.

\*Cardiovascular death occurred in 62 Taiwanese and 12 Japanese, respectively.

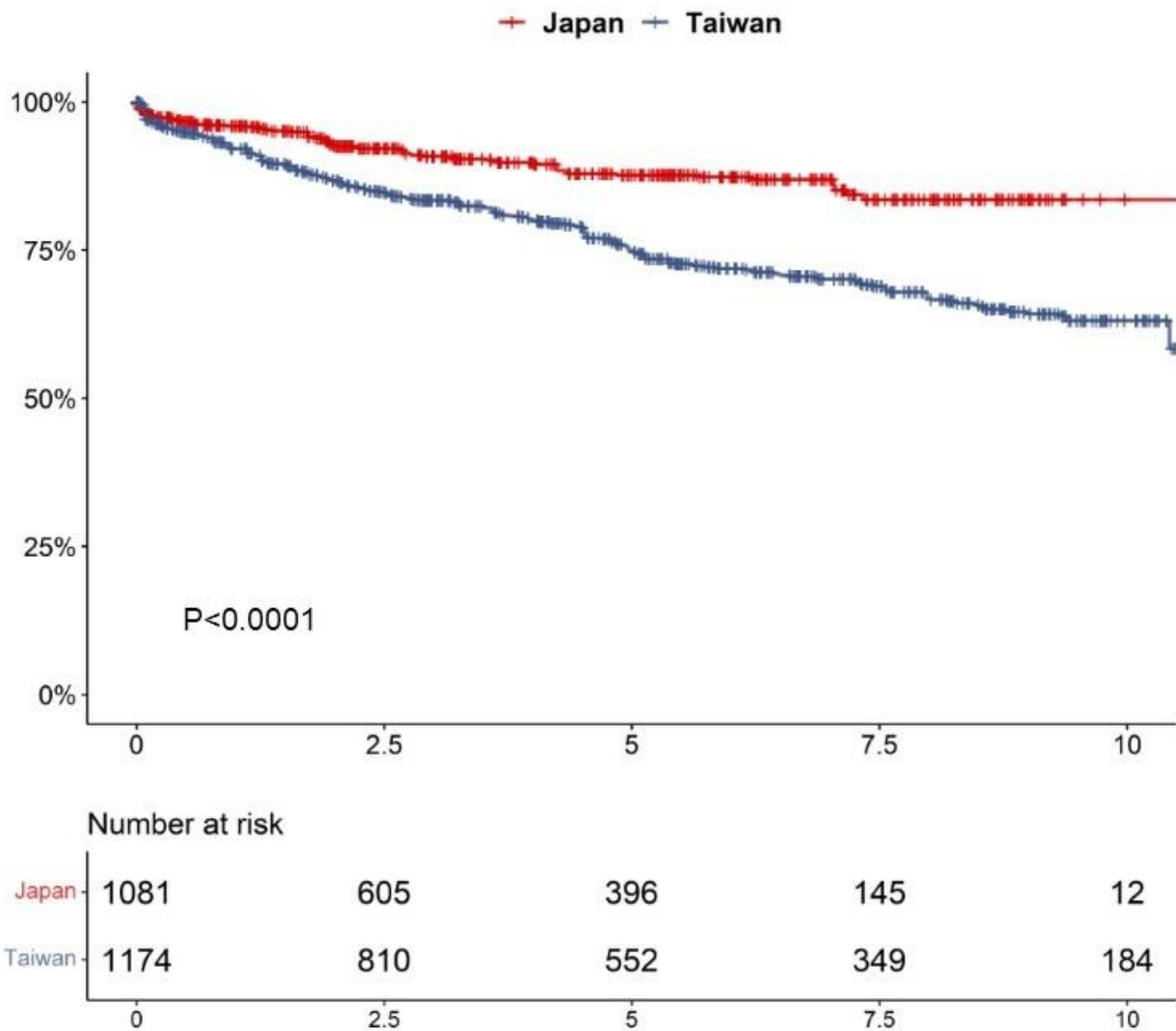
**eTable 5.** Multivariate Cox Proportional Hazards Regression Analysis for Factors Associated With Cardiovascular Death During Total Follow-Up (n=94)\*

	Total, n=1259		Taiwan, n=744		Japan, n=515	
	94 deaths		78 deaths		16 deaths	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
<b>Model 1: LVEF</b>						
Age	1.05(1.03-1.06)	<0.001	1.05(1.03-1.07)	<0.001	1.06(1.01-1.11)	<b>0.01</b>
Female	1.93(1.25-2.99)	<b>0.003</b>	1.84(1.12-3.01)	<b>0.01</b>		
Charlson comorbidity index	1.15(1.02-1.28)	<b>0.02</b>	1.07(0.93-1.22)	0.3		
NYHA (I as reference)						
II	1.34(0.81-2.24)	0.25	1.49(0.85-2.60)	0.16		
III/IV	2.61(1.36-5.03)	<b>0.004</b>	3.07(1.47-6.42)	<b>0.003</b>		
LVEF per 10%	0.72 (0.60-0.87)	<0.001	0.74(0.61-0.92)	<b>0.005</b>	0.55(0.38-0.78)	<0.001
Time-dependent AVS	0.70(0.40-1.23)	0.22	0.68(0.36-1.27)	0.22		
Taiwanese vs Japanese	3.31(1.88-5.83)	<0.001				
<b>Model 2: LVESDi</b>						
Age	1.04(1.03-1.06)	<0.001	1.05(1.03-1.07)	<0.001	1.06(1.01-1.11)	<b>0.02</b>
Female	1.73(1.12-2.67)	<b>0.01</b>	1.66(1.02-2.71)	<b>0.04</b>		
Charlson comorbidity index	1.18(1.06-1.32)	<b>0.003</b>	1.09(0.96-1.25)	0.18		
NYHA (I as reference)						
II	1.42(0.86-2.36)	0.17	1.56(0.90-2.72)	0.12		
III/IV	2.93(1.56-5.53)	<0.001	3.32(1.63-6.77)	<0.001		
LVESDi, mm/m <sup>2</sup>	1.05(1.01-1.09)	<b>0.008</b>	1.05(1.01-1.09)	<b>0.02</b>	1.07(1.00-1.15)	<b>0.04</b>
Time-dependent AVS	0.67(0.38-1.18)	0.17	0.63(0.33-1.19)	0.16		
Taiwanese vs Japanese	3.23(1.80-5.77)	<0.001				
<b>Model 3: LVESVi</b>						
Age	1.05(1.03-1.07)	<0.001	1.05(1.03-1.07)	<0.001	1.07(1.02-1.12)	<b>0.004</b>
Female	2.01(1.28-3.16)	<b>0.002</b>	1.86(1.12-3.07)	<b>0.02</b>		
Charlson comorbidity index	1.18(1.06-1.32)	<b>0.003</b>	1.10(0.96-1.25)	0.16		
NYHA (I as reference)						
II	1.38(0.83-2.30)	0.21	1.54(0.88-2.69)	0.13		
III/IV	2.82(1.48-5.36)	<b>0.002</b>	3.34(1.62-6.88)	<b>0.001</b>		
LVESVi per 10ml/m <sup>2</sup>	1.10(1.03-1.18)	<b>0.004</b>	1.08(0.99-1.17)	0.06	1.18(1.06-1.30)	<b>0.002</b>
Time-dependent AVS	0.66(0.37-1.17)	0.15	0.65(0.34-1.25)	0.16		
Taiwanese vs Japanese	3.21(1.81-5.69)	<0.001				

During total follow-up, there were 78 and 16 cardiac deaths in Taiwanese and Japanese, respectively.

\*Cardiovascular death occurred in 78 Taiwanese and 16 Japanese, respectively.

**eFigure 2. Survival between Japanese and Taiwanese individuals using inverse probability of treatment weighting (IPTW) model.** Covariates related to survival were included in the model as the following: age, sex, body surface area, New York Heart Association functional class, Charlson comorbidity index, left ventricular ejection fraction, left ventricular end-systolic dimension index, left ventricular end-systolic volume index, left atrial volume index, and aortic valve surgery. Results showed that Japanese had better survival (hazard ratio, 2.23; 95% confidence interval, 1.51-3.30).





**eTable 6:** Factors Associated With All-cause Death Under Medical Surveillance in Patients with LVEF of 50% or Greater and NYHA Class I\*

	Total, n=573		Taiwan, n=331		Japan, n=242	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
<b>Model 1: LVEF</b>						
Age	1.06(1.03-1.08)	<0.0001	1.05(1.03-1.08)	<0.0001	1.12(1.02-1.26)	0.004
Charlson comorbidity index	1.29(1.14-1.45)	0.0002	1.21(1.03-1.39)	0.01	1.57(1.23-1.98)	0.0006
Taiwanese vs Japanese	1.89(0.993-5.8)	0.04				
LVEF per 10%	0.88(0.58-1.32)	0.55	1.10(0.69-1.75)	0.66	0.35(0.07-1.19)	0.10
<b>Model 2: LVESDi</b>						
Age	1.06(1.03-1.09)	<0.0001	1.05(1.03-1.08)	<0.0001	1.14(1.03-1.29)	0.002
Charlson comorbidity index	1.27(1.12-1.43)	0.0003	1.19(1.02-1.36)	0.02	1.70(1.31-2.19)	0.0002
Taiwanese vs Japanese	2.49(1.294-8.0)	0.003				
LVESDi, mm/m <sup>2</sup>	1.11(1.03-1.19)	0.003	1.10(1.01-1.19)	0.02	1.18(1.02-1.36)	0.02
<b>Model 3: LVESVi</b>						
Age	1.07(1.04-1.09)	<0.0001	1.06(1.03-1.09)	<0.0001	1.14(1.04-1.28)	0.0007
Charlson comorbidity index	1.27(1.12-1.42)	0.0003	1.19(1.02-1.36)	0.02	1.70(1.33-2.15)	<0.0001
Taiwanese vs Japanese	2.39(1.24-4.58)	0.008				
LVESVi per 10ml/m <sup>2</sup>	1.36(1.10-1.65)	0.003	1.25(0.98-1.57)	0.06	1.93(1.20-3.10)	0.006

Sex was not associated with all-cause death univariably thus was not included in the models.

\*All-cause mortality (n=63) occurred in 50 Taiwanese and 13 Japanese, respectively.

**eTable 7.** Comparison between Asian and Western Individuals\*

	Asians, n=1259	Westerners, n=1072*
<b>Baseline demography</b>		
Age, year	64±17	59±18
Female	325(26)	189(18)
Body surface area, m <sup>2</sup>	1.67±0.21	2.0±0.2
Charlson index	1.28±1.71	1.06 ± 1.25
Diastolic blood pressure, mmHg	65±13	64±13
NYHA <sup>†</sup> (1245/1050)	700(56)	675(64)
I		
II	418(34)	267(25)
III+IV	127(10)	108(10)
BAV fusion, RL fusion	177(73)	308(82)
RN	50(21)	63(17)
LN	15(6)	6(1)
LVEF, %	55±11	59±9
LVEDD, mm	60±8	60±7
LVESD, mm	41±9	40±7
LVEDDi, mm/m <sup>2</sup>	36.6±5.2	30.3±4.1
LVESDi, mm/m <sup>2</sup>	24.7±5.7	20.2±3.8
LVESDi>25 mm/m <sup>2</sup>	481(38)	107(10)
LVEDVi, ml/m <sup>2</sup> (n=1247/1007)	108±39	103±31
LVESVi, ml/m <sup>2</sup> (n=1245/1007)	50±28	44±20
Annulus, mm	23.4±3.2	26±3
Indexed Annulus	14.2±1.9	13.0±1.6
Sinus of Valsalva, mm	40.5±8.2	41±6
Indexed Sinus of Valsalva	24.4±4.9	20.3±3.2
Mid-ascending aorta, mm	40.4±8.1	41±7
Indexed Mid-ascending aorta	24.7±5.5	20.4±4.4
<b>Surgical indications (481<sup>†</sup>/552)</b>		
Symptoms	285(59)	345(63)
LVEF<50%	47(10)	23(4)
LVESD(i) >50mm(25mm/m <sup>2</sup> )	75(16)	21(3.8)
Aortic aneurysm	21(4)	59(11)
LVEDD>65mm	36(7)	62(11)
Early surgery	17(4)	42(8)
Aortic valve repair	24(5)	122(22)
Bioprosthesis	330(72)	234(54)
Concomitant aorta surgery	170(35)	175(32)

Concomitant coronary artery bypass grafting	48(10)	86(16)
8-year incidence of aortic valve surgery <sup>§</sup>	48±2%	55±2%
8-year survival of total follow-up <sup>§</sup>	74±2%	78±2%
8-year survival under medical surveillance <sup>§</sup>	68±2%	72±2%
8-year post-AVS survival <sup>§</sup>	85±3%	84±2%

See Table 1 for abbreviations.

\*Western cohort was from Yang LT et al. *J Am Coll Cardiol.* 2020 Jul 21;76(3):233-246.

†Patients with undetermined NYHA status were excluded.

‡Of 483 patients having aortic valve surgery, 2 had it performed elsewhere hence surgical indications were lacking.

§For ease of comparison, data at 8-year was shown.