

## Supplementary data

**Supplementary Table 1. Baseline characteristics of high-gradient aortic stenosis.**

	Total	Early stage	Advanced stage	P-value
	N=1045	N=516	N=529	
Age, years	82.4 ± 5.9	82.3 ± 5.5	82.6 ± 6.3	0.349
Female, n (%)	565 (54.1)	267 (51.7)	298 (56.3)	0.137
Body mass index, kg/cm <sup>2</sup>	26.4 ± 5.5	26.6 ± 5.6	26.1 ± 5.5	0.099
STS-PROM, %	5.4 ± 4.1	4.7 ± 3.1	6.2 ± 4.7	<0.001
NYHA III or IV, n (%)	679 (65.0)	316 (61.2)	363 (68.6)	0.012
<b>Concomitant diseases</b>				
Hypertension, n (%)	882 (84.4)	436 (84.5)	446 (84.3)	0.934
Diabetes mellitus, n (%)	256 (24.5)	113 (21.9)	143 (27.0)	0.054
CKD (eGFR <60 mL/min/1.73 m <sup>2</sup> ), n (%)	720 (69.0)	331 (64.3)	389 (73.5)	0.001
eGFR, mL/min/1.73 m <sup>2</sup>	52.5 ± 21.7	55.0 ± 22.1	50.0 ± 21.0	<0.001
COPD, n (%)	114 (10.9)	49 (9.5)	65 (12.3)	0.145
Coronary artery disease, n (%)	580 (55.5)	275 (53.3)	305 (57.7)	0.156
Atrial fibrillation, n (%)	311 (29.8)	124 (24.0)	187 (35.3)	<0.001
<b>Previous history</b>				
Previous myocardial infarction, n (%)	120 (11.5)	45 (8.7)	75 (14.2)	0.006
Previous cardiac surgery, n (%)	109 (10.4)	43 (8.3)	66 (12.5)	0.028
Previous stroke, n (%)	115 (11.0)	60 (11.6)	55 (10.4)	0.525
Previous permanent pacemaker implantation, n (%)	63 (6.0)	23 (4.5)	40 (7.6)	0.035
Peripheral artery disease, n (%)	138 (13.2)	60 (11.6)	78 (14.7)	0.137
<b>Echocardiography</b>				

Aortic Valve Area, cm <sup>2</sup>	0.63 ± 0.23	0.65 ± 0.21	0.61 ± 0.24	0.002
Mean Aortic valve pressure gradient, mmHg	53 ± 13	53 ± 12	54 ± 14	0.255
Left ventricular ejection fraction, %	57 ± 13	61 ± 10	53 ± 14	<0.001
Left ventricular mass index, g/m <sup>2</sup>	139 ± 44	134 ± 44	143 ± 46	0.004
Left atrial volume index, mL/m <sup>2</sup>	43 ± 16	41 ± 14	46 ± 17	<0.001
Mitral regurgitation ≥moderate, n (%)	217 (21.0)	58 (11.4)	159 (30.4)	<0.001
Tricuspid regurgitation ≥moderate, n (%)	161 (15.6)	0 (0)	161 (30.6)	<0.001
Systolic pulmonary artery pressure, mmHg	46 ± 18	37 ± 15	56 ± 17	<0.001
Tricuspid annular plane systolic excursion, cm	21 ± 5	23 ± 4	19 ± 6	<0.001
Stroke volume index, mL/m <sup>2</sup>	34 ± 12	35 ± 11	33 ± 12	0.005
<b>Computed tomography</b>				
Aortic valvular complex calcification, mm <sup>3</sup>	442.4 ± 423.8	429.0 ± 379.7	456.8 ± 466.8	0.324
<b>Right heart catheterisation</b>				
Mean pulmonary artery pressure, mmHg	31 ± 12	25 ± 9	36 ± 13	<0.001
STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; NYHA = New York Heart Association; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; COPD = chronic obstructive pulmonary disease.				

**Supplementary Table 2. Baseline characteristics of classical low-flow low-gradient aortic stenosis.**

	Total	Early stage	Advanced stage	P-value
	N=337	N=89	N=248	
Age, years	81.0 ± 7.5	82.0 ± 6.8	80.8 ± 7.7	0.182
Female, n (%)	109 (32.3)	27 (30.3)	82 (33.1)	0.637
Body mass index, kg/cm <sup>2</sup>	25.8 ± 5.2	26.5 ± 5.0	25.5 ± 5.3	0.124
STS-PROM, %	7.0 ± 5.3	6.2 ± 4.9	7.3 ± 5.4	0.120
NYHA III or IV, n (%)	262 (78.0)	64 (71.9)	198 (80.2)	0.107
<b>Concomitant diseases</b>				
Hypertension, n (%)	289 (85.8)	80 (89.9)	209 (84.3)	0.194
Diabetes mellitus, n (%)	113 (33.5)	28 (31.5)	85 (34.3)	0.630
CKD (eGFR <60 mL/min/1.73 m <sup>2</sup> ), n (%)	238 (70.6)	56 (62.9)	182 (73.4)	0.063
eGFR, mL/min/1.73 m <sup>2</sup>	50.2 ± 22.1	53.3 ± 22.4	49.1 ± 22.0	0.116
COPD, n (%)	47 (14.0)	12 (13.5)	35 (14.2)	0.873
Coronary artery disease, n (%)	231 (68.5)	66 (74.2)	165 (66.5)	0.184
Atrial fibrillation, n (%)	161 (47.8)	34 (38.2)	127 (51.2)	0.035
<b>Previous history</b>				
Previous myocardial infarction, n (%)	97 (28.8)	29 (32.6)	68 (27.4)	0.356
Previous cardiac surgery, n (%)	81 (24.0)	17 (19.1)	64 (25.8)	0.204
Previous stroke, n (%)	52 (15.4)	12 (13.5)	40 (16.1)	0.553
Previous permanent pacemaker implantation, n (%)	49 (14.5)	8 (9.0)	41 (16.5)	0.083
Peripheral artery disease, n (%)	61 (18.1)	15 (16.9)	46 (18.5)	0.722
<b>Echocardiography</b>				
Aortic Valve Area, cm <sup>2</sup>	0.76 ± 0.28	0.78 ± 0.25	0.76 ± 0.30	0.658
Mean Aortic valve pressure gradient, mmHg	24 ± 9	26 ± 8	23 ± 9	0.008

Left ventricular ejection fraction, %	32 ± 11	35 ± 10	31 ± 12	0.004
Left ventricular mass index, g/m <sup>2</sup>	147 ± 51	150 ± 59	146 ± 47	0.564
Left atrial volume index, mL/m <sup>2</sup>	49 ± 23	41 ± 13	53 ± 25	<0.001
Mitral regurgitation ≥moderate, n (%)	141 (42.7)	28 (32.9)	113 (46.1)	0.034
Tricuspid regurgitation ≥moderate, n (%)	90 (27.4)	0 (0)	90 (37.0)	<0.001
Systolic pulmonary artery pressure, mmHg	49 ± 19	34 ± 15	55 ± 16	<0.001
Tricuspid annular plane systolic excursion, cm	17 ± 6	22 ± 4	15 ± 5	<0.001
Stroke volume index, mL/m <sup>2</sup>	25 ± 6	27 ± 5	24 ± 6	<0.001
<b>Computed tomography</b>				
Aortic valvular complex calcification, mm <sup>3</sup>	213.2 ± 229.9	233.7 ± 264.3	204.5 ± 213.5	0.028
<b>Right heart catheterisation</b>				
Mean pulmonary artery pressure, mmHg	34 ± 12	23 ± 8	37 ± 11	<0.001
STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; NYHA = New York Heart Association; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; COPD = chronic obstructive pulmonary disease.				

**Supplementary Table 3. Baseline characteristics of low-flow low-gradient aortic stenosis with preserved ejection fraction.**

	Total	Early stage	Advanced stage	P-value
	N=394	N=175	N=219	
Age, years	82.0 ± 6.6	81.9 ± 6.4	82.1 ± 6.8	0.844
Female, n (%)	220 (55.8)	93 (53.1)	127 (57.9)	0.094
Body mass index, kg/cm <sup>2</sup>	27.0 ± 5.7	27.1 ± 5.7	26.9 ± 5.7	0.674
STS-PROM, %	5.1 ± 3.2	4.7 ± 2.6	5.5 ± 3.5	0.009
NYHA III or IV, n (%)	273 (69.3)	120 (68.6)	153 (69.9)	0.782
<b>Concomitant diseases</b>				
Hypertension, n (%)	342 (86.8)	152 (86.9)	190 (86.8)	0.977
Diabetes mellitus, n (%)	116 (29.4)	50 (28.6)	66 (30.1)	0.735
CKD (eGFR <60 mL/min/1.73 m <sup>2</sup> ), n (%)	267 (67.8)	119 (68.0)	148 (67.6)	0.929
eGFR, mL/min/1.73 m <sup>2</sup>	53.1 ± 21.6	53.9 ± 20.5	52.3 ± 22.6	0.480
COPD, n (%)	61 (15.5)	23 (13.1)	38 (17.4)	0.251
Coronary artery disease, n (%)	240 (60.9)	115 (65.7)	125 (57.1)	0.081
Atrial fibrillation, n (%)	167 (42.4)	46 (26.3)	121 (55.3)	<0.001
<b>Previous history</b>				
Previous myocardial infarction, n (%)	51 (12.9)	25 (14.3)	26 (11.9)	0.478
Previous cardiac surgery, n (%)	64 (16.2)	23 (13.1)	41 (18.7)	0.136
Previous stroke, n (%)	49 (12.4)	21 (12.0)	28 (12.8)	0.814
Previous permanent pacemaker implantation, n (%)	42 (10.7)	14 (8.0)	28 (12.8)	0.126
Peripheral artery disease, n (%)	57 (14.5)	26 (14.9)	31 (14.2)	0.844
<b>Echocardiography</b>				
Aortic Valve Area, cm <sup>2</sup>	0.77 ± 0.26	0.76 ± 0.26	0.78 ± 0.26	0.466
Mean Aortic valve pressure gradient, mmHg	27 ± 8	27 ± 8	27 ± 8	0.518

Left ventricular ejection fraction, %	61 ± 7	63 ± 7	60 ± 7	<0.001
Left ventricular mass index, g/m <sup>2</sup>	121 ± 41	119 ± 39	124 ± 41	0.304
Left atrial volume index, mL/m <sup>2</sup>	42 ± 17	37 ± 14	46 ± 18	<0.001
Mitral regurgitation ≥moderate, n (%)	80 (20.6)	18 (10.3)	62 (29.0)	<0.001
Tricuspid regurgitation ≥moderate, n (%)	84 (21.6)	0 (0)	84 (39.1)	<0.001
Systolic pulmonary artery pressure, mmHg	46 ± 18	37 ± 13	53 ± 18	<0.001
Tricuspid annular plane systolic excursion, cm	19 ± 5	22 ± 4	17 ± 5	<0.001
Stroke volume index, mL/m <sup>2</sup>	26 ± 6	26 ± 6	26 ± 6	0.784
<b>Computed tomography</b>				
Aortic valvular complex calcification, mm <sup>3</sup>	206.3 ± 273.2	225.4 ± 244.5	189.1 ± 296.4	0.218
<b>Right heart catheterisation</b>				
Mean pulmonary artery pressure, mmHg	30 ± 12	24 ± 8	34 ± 13	<0.001
STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; NYHA = New York Heart Association; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; COPD = chronic obstructive pulmonary disease.				

**Supplementary Table 4. Baseline characteristics of normal-flow low-gradient aortic stenosis.**

	Total	Early stage	Advanced stage	P-value
	N=314	N=152	N=162	
Age, years	81.5 ± 6.3	81.0 ± 6.5	82.0 ± 6.0	0.142
Female, n (%)	155 (49.4)	70 (46.1)	85 (52.5)	0.256
Body mass index, kg/cm <sup>2</sup>	25.9 ± 5.1	25.4 ± 4.7	26.4 ± 5.4	0.083
STS-PROM, %	5.1 ± 3.5	4.8 ± 3.5	5.4 ± 3.5	0.114
NYHA III or IV, n (%)	197 (62.7)	85 (55.9)	112 (69.1)	0.016
<b>Concomitant diseases</b>				
Hypertension, n (%)	280 (89.2)	128 (84.2)	152 (93.8)	0.006
Diabetes mellitus, n (%)	76 (24.2)	33 (21.7)	43 (26.5)	0.318
CKD (eGFR <60 mL/min/1.73 m <sup>2</sup> ), n (%)	219 (70.0)	100 (65.8)	119 (73.9)	0.117
eGFR, mL/min/1.73 m <sup>2</sup>	50.6 ± 22.5	52.8 ± 22.9	48.1 ± 22.0	0.069
COPD, n (%)	43 (13.7)	21 (13.9)	22 (13.6)	0.933
Coronary artery disease, n (%)	194 (61.8)	83 (54.6)	111 (68.5)	0.011
Atrial fibrillation, n (%)	104 (33.1)	46 (30.3)	58 (35.8)	0.297
<b>Previous history</b>				
Previous myocardial infarction, n (%)	40 (12.7)	16 (10.5)	24 (14.8)	0.225
Previous cardiac surgery, n (%)	57 (18.2)	20 (13.2)	37 (22.8)	0.026
Previous stroke, n (%)	44 (14.0)	23 (15.1)	21 (13.0)	0.580
Previous permanent pacemaker implantation, n (%)	28 (8.9)	11 (7.2)	17 (10.5)	0.312
Peripheral artery disease, n (%)	43 (13.7)	24 (15.8)	19 (11.7)	0.296
<b>Echocardiography</b>				
Aortic Valve Area, cm <sup>2</sup>	0.85 ± 0.30	0.81 ± 0.29	0.88 ± 0.31	0.037
Mean Aortic valve pressure gradient, mmHg	28 ± 9	29 ± 8	27 ± 9	0.003

Left ventricular ejection fraction, %	63 ± 7	64 ± 7	62 ± 7	0.040
Left ventricular mass index, g/m <sup>2</sup>	124 ± 41	122 ± 38	126 ± 44	0.527
Left atrial volume index, mL/m <sup>2</sup>	42 ± 24	37 ± 12	47 ± 32	<0.001
Mitral regurgitation ≥moderate, n (%)	59 (19.2)	12 (8.0)	47 (29.7)	<0.001
Tricuspid regurgitation ≥moderate, n (%)	52 (16.7)	0 (0)	52 (32.3)	<0.001
Systolic pulmonary artery pressure, mmHg	43 ± 16	35 ± 13	50 ± 15	<0.001
Tricuspid annular plane systolic excursion, cm	21 ± 5	23 ± 4	20 ± 6	<0.001
Stroke volume index, mL/m <sup>2</sup>	45 ± 12	45 ± 11	45 ± 12	0.698
<b>Computed tomography</b>				
Aortic valvular complex calcification, mm <sup>3</sup>	200.3 ± 203.6	224.7 ± 215.5	173.9 ± 187.2	0.039
<b>Right heart catheterisation</b>				
Mean pulmonary artery pressure, mmHg	28 ± 9	23 ± 7	32 ± 9	<0.001
STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; NYHA = New York Heart Association; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; COPD = chronic obstructive pulmonary disease.				



**Supplementary Table 5. Clinical outcomes according to four cardiac stages in each AS subtype.**

	HG-AS	Classical LF-LG	LF LG-AS with pEF	NFLG
	N=1045	N=337	N=394	N=314
<b>All-cause mortality at 1 year</b>				
Stage 0 and 1, n (%)	5 (3.6%) reference	2 (20.0%) reference	6 (9.8%) reference	5 (10.2%) reference
Stage 2, n (%)	30 (8.6%) HR 2.14 [0.83-5.54] <i>P</i> = 0.117	5 (7.8%) HR 0.35 [0.07-1.81] <i>P</i> = 0.210	11 (10.5%) HR 0.85 [0.31-2.35] <i>P</i> = 0.754	10 (11.6%) HR 1.06 [0.35-3.19] <i>P</i> = 0.920
Stage 3, n (%)	43 (16.6%) HR 3.73 [1.45-9.59] <i>P</i> = 0.006	13 (23.6%) HR 1.05 [0.23-4.72] <i>P</i> = 0.948	19 (20.0%) HR 1.34 [0.52-3.47] <i>P</i> = 0.544	12 (14.6%) HR 1.40 [0.49-4.01] <i>P</i> = 0.532
Stage 4, n (%)	46 (22.7%) HR 5.46 [2.11-14.13] <i>P</i> <0.001	44 (30.6%) HR 1.54 [0.36-6.56] <i>P</i> = 0.560	23 (24.5%) HR 1.64 [0.63-4.25] <i>P</i> = 0.311	11 (20.4%) HR 1.32 [0.45-3.92] <i>P</i> = 0.615
<b>Cardiovascular mortality at 1 year</b>				
Stage 0 and 1, n (%)	3 (2.1%) reference	0 (0%)	3 (4.9%) reference	1 (2.0%) reference
Stage 2, n (%)	18 (5.1%) HR 2.00 [0.58-6.84] <i>P</i> = 0.270	4 (6.3%) reference	8 (7.6%) HR 1.14 [0.30-4.37] <i>P</i> = 0.852	4 (4.7%) HR 2.41 [0.26-22.44] <i>P</i> = 0.441
Stage 3, n (%)	28 (10.8%) HR 3.54 [1.05-11.98] <i>P</i> = 0.042	8 (14.5%) HR 2.37 [0.72-7.68] <i>P</i> = 0.178	13 (13.7%) HR 1.69 [0.46-6.15] <i>P</i> = 0.427	8 (9.8%) HR 5.56 [0.68-45.30] <i>P</i> = 0.109
Stage 4, n (%)	31 (15.3%) HR 5.50 [1.62-18.66] <i>P</i> = 0.006	36 (25.0%) HR 4.38 [1.48-11.97] <i>P</i> = 0.008	18 (19.1%) HR 2.25 [0.62-8.15] <i>P</i> = 0.216	6 (11.1%) HR 3.59 [0.41-31.46] <i>P</i> = 0.248

<b>All-cause mortality at 5 year</b>				
Stage 0 and 1, n (%)	34 (26.7%) reference	6 (66.0%) reference	18 (34.3%) reference	14 (33.5%) reference
Stage 2, n (%)	130 (41.7%) HR 1.54 [1.05-2.25] <i>P</i> = 0.026	31 (54.4%) HR 0.62 [0.25-1.50] <i>P</i> = 0.287	45 (46.2%) HR 1.23 [0.70-2.15] <i>P</i> = 0.477	27 (35.8%) HR 0.92 [0.48-1.77] <i>P</i> = 0.796
Stage 3, n (%)	129 (57.0%) HR 2.35 [1.59-3.46] <i>P</i> <0.001	31 (67.2%) HR 0.81 [0.33-1.98] <i>P</i> = 0.643	51 (61.2%) HR 1.88 [1.08-3.28] <i>P</i> = 0.027	29 (47.6%) HR 1.36 [0.71-2.59] <i>P</i> = 0.359
Stage 4, n (%)	104 (54.8%) HR 2.28 [1.51-3.43] <i>P</i> <0.001	83 (64.5%) HR 1.00 [0.42-2.35] <i>P</i> = 0.996	55 (66.7%) HR 2.02 [1.16-3.52] <i>P</i> = 0.013	26 (50.4%) HR 1.31 [0.66-2.57] <i>P</i> = 0.439
<b>Cardiovascular mortality at 5 year</b>				
Stage 0 and 1, n (%)	23 (19.3%) reference	3 (52.9%) reference	10 (21.1%) reference	7 (18.9%) reference
Stage 2, n (%)	80 (29.8%) HR 1.41 [0.88-2.25] <i>P</i> = 0.149	23 (42.1%) HR 0.86 [0.26-2.91] <i>P</i> = 0.811	34 (38.4%) HR 1.54 [0.75-3.16] <i>P</i> = 0.241	18 (27.6%) HR 1.19 [0.49-2.88] <i>P</i> = 0.706
Stage 3, n (%)	93 (48.0%) HR 2.47 [1.54-3.94] <i>P</i> <0.001	22 (58.1%) HR 1.11 [0.33-3.78] <i>P</i> = 0.865	38 (52.0%) HR 2.45 [1.19-5.05] <i>P</i> = 0.015	20 (36.6%) HR 1.76 [0.74-4.18] <i>P</i> = 0.204
Stage 4, n (%)	73 (44.7%) HR 2.45 [1.49-4.03] <i>P</i> <0.001	69 (58.4%) HR 1.53 [0.47-5.00] <i>P</i> = 0.479	36 (50.2%) HR 2.25 [1.09-4.65] <i>P</i> = 0.029	18 (39.3%) HR 1.54 [0.62-3.81] <i>P</i> = 0.351
AS = aortic stenosis; HG = high gradient; LG = low gradient; LF = classical low flow; NF = normal flow; pEF = preserved ejection fraction; HR = hazard ratio. HR was adjusted by age, sex, Society of Thoracic Surgeons Predicted Risk of Mortality, left ventricular rejection fraction, New York Heart Association class III or IV, estimated glomerular filtration rate, and the year of transcatheter aortic valve implantation.				

**Supplementary Table 6. Comparison of baseline characteristics between included and excluded patients.**

	Included patients	Excluded patients	p-value
	N = 2090	N = 1496	
Age, years	82.0 ± 6.4	81.6 ± 6.3	0.007
Female, n (%)	1046 (50.1)	696 (46.4)	0.029
Body mass index, kg/cm <sup>2</sup>	26.5 ± 5.2	27.0 ± 5.4	0.009
STS-PROM, %	5.8 ± 4.1	4.5 ± 3.8	<0.001
NYHA III or IV, n (%)	1410 (67.6)	874 (58.4)	<0.001
<b>Concomitant diseases</b>			
Hypertension, n (%)	1791 (85.8)	1343 (89.6)	<0.001
Diabetes mellitus, n (%)	561 (26.9)	413 (27.6)	0.656
CKD (eGFR <60 mL/min/1.73 m <sup>2</sup> ), n (%)	1442 (69.2)	938 (62.7)	<0.001
eGFR, mL/min/1.73 m <sup>2</sup>	51.4 ± 21.6	52.1 ± 22.2	0.433
COPD, n (%)	264 (12.7)	132 (8.8)	<0.001
Coronary artery disease, n (%)	1245 (59.7)	828 (55.2)	0.008
Atrial fibrillation, n (%)	742 (35.6)	466 (31.1)	0.005
<b>Previous history</b>			
Previous myocardial infarction, n (%)	308 (14.8)	188 (12.5)	0.058
Previous cardiac surgery, n (%)	311 (14.9)	205 (13.7)	0.302
Previous stroke, n (%)	260 (12.5)	172 (11.5)	0.372
Previous permanent pacemaker implantation, n (%)	182 (8.7)	116 (7.7)	0.293
Peripheral artery disease, n (%)	299 (14.3)	165 (11.0)	0.003
<b>Echocardiography</b>			
Left ventricular ejection fraction, %	54 ± 14	56 ± 14	0.005
Aortic Valve Area, cm <sup>2</sup>	0.73 ± 0.25	0.80 ± 0.28	<0.001
Mean Aortic valve pressure gradient, mmHg	40 ± 17	39 ± 17	0.344

AS = aortic stenosis; HG = high gradient; LG = low gradient; LF = classical low flow; NF = normal flow; pEF = preserved ejection fraction; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; NYHA = New York Heart Association; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; COPD = chronic obstructive pulmonary disease.