APPENDIX

Table A1 Characteristics in those who showed a relative increase or decrease in pVO_2 >10% from pre- to post-AVR

	Relative increase in pVO_2>10% N=9	**Relative decrease in pVO_2>10%** N=11
PreAVR		
Age (years)	71.7 (6.2)	67.6 (12.5)
Male/female (n)	8/1	7/4
Atrial fibrillation (n)	1	3
Diabetes mellitus (n)	2	0
Hypertension (n)	3	9
COPD (n)	0	2
Clinical findings/symptoms leading to AVR		
New or worsening dyspnoea/angina	3	6
Equivocal symptomatic from dyspnoea/angina and symptoms revealed during CPX	5	2
Equivocal symptomatic from dyspnoea/angina with low pVO_2 not explained by other causes	1	2
Hospitalization for heart failure	0	1
AVAI (cm^2/m^2)	0.34 (0.06)	0.46 (0.15)
Peak gradient (mm Hg)	79.7 (18.9)	67.4 (24.1)
Mean gradient (mm Hg)	49.8 (14.4)	40.3 (14.9)
Sa (cm/s)	4.8 (0.5)	4.5 (1.3)
E/e'	16.3 (5.2)	14.7 (4.5)
pVO_2 (mL/kg)	16.4 (3.7)	17.4 (5.6)
% achieved of predicted pVO_2 (%)	78.5 (12.4)	79.4 (20.7)
pO_2pulse (mL/beat)	11.7 (3.1)	10.9 (2.7)
% of predicted pO_2pulse (%)	87.9 (18.2)	94.7 (19.9)
BNP>ULN	2	5
Ratio BNP/ULN of BNP (median and range)	0.48 (0.15-2.56)	1.24 (0.20-4.76)
On Beta-blocker (n)	2	5
Pacemaker (n)	1	2
PostAVR		
SAVR/TAVR (n)	7/2	6/5
On Beta-blocker (n)	1	7
Pacemaker (n)	2	5
Change in Hb (mmol/l)	-0.08 (0.48)	-0.58 (0.75)
Days in hospital (median/range)	10 (5-18)	16 (5-52)
BNP>ULN	2	7
Ratio BNP/ULN of BNP (median and range)	0.22 (0.09-4.93)	1.17 (0.26-3.05)
Mean gradient (mm Hg)	15.2 (4.1)	12.5 (4.7)
Sa (cm/s)	5.8 (1.4)	5.3 (1.8)
Change in Sa (cm/s)	1.0 (1.2)	0.5 (1.1)
E/e´	9.9 (4.2)	13.9 (5.7)
Change in E/e´	-6.0 (5.3)	-0.54 (5.5)

Table A2. Univariate explanatory variables for a relative increase or decrease in pVO_2 >10%

Explanatory variable	Relative increase in pVO_2>10%			Relative decrease in pVO_2>10%		
	OR	CI	P-value	OR	CI	P-value
PreAVR						
Age (per year)	0.97	0.89-1.06	0.49	0.97	0.90-1.04	0.39
Male vs. female	4.44	0.48-41.7	0.19	0.65	0.14-2.90	0.57
Atrial fibrillation	0.31	0.03-2.92	0.30	1.25	0.25-6.5	0.79
COPD	N/A	N/A	0.99	1.70	0.25-11.9	0.59
Hypertension	0.24	0.05-1.17	0.077	4.50	0.81-25.0	0.09
Mean gradient (per mm Hg)	0.99	0.95-1.05	0.86	0.93	0.86-0.99	0.033
Mean gradient <40 mm Hg	0.37	0.04-3.55	0.39	14.40	2.2-93.2	0.005
AVAI (per 0.1cm^2/m^2)	0.25	0.07-0.92	0.037	1.68	0.87-3.26	0.13
AVAI<0.4cm^2/m^2	9.23	1.02-83.9	0.048	0.52	0.13-2.17	0.37
Sa (per 1cm/s)	1.03	0.56-1.87	0.94	0.76	0.43-1.33	0.33
E/e' (per unit)	1.00	0.86-1.17	0.98	0.92	0.79-1.06	0.25
BNP>ULN	0.36	0.06-2.05	0.25	0.53	0.12-2.33	0.40
Ln BNP/ULN of BNP	0.53	0.24-1.19	0.12	0.54	0.74-3.21	0.25
pVO_2 (per mL/kg)	1.12	0.95-1.33	0.19	0.95	0.82-1.09	0.44
% of predicted pVO_2 (per %)	1.04	0.99-1.09	0.14	0.97	0.92-1.01	0.13
% of predicted pO_2pulse (per 1%)	0.96	0.92-1.00	0.074	0.98	0.95-1.02	0.35
pO_2pulse <median value (98% of predicted)	4.67	0.82-26.3	0.083	0.49	0.60-2.09	0.34
On beta-blocker	0.51	0.09-2.96	0.46	2.26	0.52-9.80	0.28
PostAVR						
SAVR vs. TAVR	1.23	0.20-7.35	0.82	0.23	0.05-1.13	0.07
On beta-blocker	0.09	0.01-0.85	0.036	2.80	0.65-12.1	0.17
Pacemaker	0.95	0.16-5.85	0.96	6.37	1.18-34.5	0.031
Change in Hb (per mmol/l)	2.78	0.65-11.9	0.17	0.353	0.10-1.22	0.10
BNP>ULN	0.31	0.05-1.76	0.19	5.25	1.08	0.041
Ln BNP/ULN of BNP	0.49	0.23-1.05	0.07	1.82	0.86-3.86	0.12
Ln days in hospital	0.41	0.08-2.18	0.29	5.01	1.03-25.0	0.046
Mean gradient	1.03	0.90-1.19	0.65	0.88	0.75-1.04	0.15
Sa (per 1cm/s)	1.10	0.69-1.75	0.70	0.85	0.55-1.32	0.47
Change in Sa	1.28	0.61-2.67	0.51	0.75	0.39-1.44	0.38
E/e' (per unit)	0.086	0.72-1.03	0.095	1.04	0.92-1.18	0.50
Change in E/e	0.90	0.77-1.05	0.17	1.14	0.98-1.31	0.094

Table A3.

Pre and postAVR characteristics in study population compared to patients who had AVR without a preAVR CPX during the study period.

	Study Group n=37	Reference Group n=36	p-value
PreAVR	,		
Age (years) (median, range)	72 (46-83)	74 (46-85)	0.2*
Male /female (n)	26/11 (70/30%)	21/15 (58/42%)	0.3
Diabetes Mellitus (n)	4 (11%)	6 (17%)	0.5
Hypertension (n)	22 (60%)	25 (70%)	0.5
Chronic obstructive pulmonary disease (n)	5 (14%)	6 (17%)	0.8
Prior PCI/CABG (n)	4 (11%)	3 (8%)	1.0
Atrial Fibrillation (n)	9 (24%)	7 (19%)	0.8
Mean gradient (mm Hg)	49.1 (15.3)	49.3 (16.4)	1.0
AVAI (cm^2/m^2)	0.41 (0.11)	0.37 (0.07)	0.07
NYHA ≥II (n)	27 (72.9%)	36 (100%)	0.002
PostAVR			
TAVR	9 (24%)	11 (31%)	0.6
pVO_2 (mL/min/kg)	18.4 (5.9)	17.6 (4.3)	0.5
% of predicted pVO_2 (%)	86.8 (22.9)	91.7 (16.9)	0.3
pO_2pulse/Hb index (mL/m^2)	42.8 (8.36)	45.7 (9.8)	0.17
% of predicted pO_2pulse (%)	104.3 (24.5)	115.2 (20.7)	0.044
Respiratory coefficient	1.06 (0.11)	1.10 (0.09)	0.11
Anaerobic threshold % of predicted pVO_2 (%)	56.0 (11.4)	60.5 (14.5)	0.14
% of predicted pHR (%)	84.1 (16.2)	81.0 (16.0)	0.4
% of predicted FEV1 (%)	83.5 (20.8)	88.5 (24.5)	0.4
AVAI (cm^2/m^2)	0.76 (0.16)	0.78 (0.26)	0.6
Sa (cm/s)	5.59 (1.64)	5.46 (1.68)	0.7
E/e’	12.9 (5.9)	11.9 (5.1)	0.4
SF-36 PCS	42.7 (9.6)	44.5 (9.3)	0.4
NYHA ≥II (n)	15 (41%)	20 (56%)	0.3
BNP > ULN (n)	15/36 (42%)	14/34 (41%)	1.0
Hb (mmol/L)	8.3 (0.9)	8.3 (0.9)	1.0
Atrial fibrillation (n)	8 (22%)	8 (22%)	1.0
Pacemaker (n)	8 (22%)	5 (14%)	0.5
Beta blockers (n)	17 (46%)	18 (50%)	0.8

Values are mean (SD) if else not indicated. *Kolmogorov-Smirnov test.

Representativeness of the study patients

Pre- and post-AVR characteristics in the study population compared to patients who had AVR without a pre-AVR CPX during the study period (Reference group) are shown in Table A3 (appendix). There were no significant differences in important pre-AVR characteristics between the study group and the reference group, besides that 27% were deemed NYHA I in the study group vs. none in the reference group. Post AVR, the achieved predicted pO_2pulse was slightly higher in the reference group, which may partly be explained by lower peak heart rates or by chance (multiple comparisons).

Most patients with aortic stenosis who are referred for AVR in our region (800.000 inhabitants) are evaluated at our institution. From the National Heart Registry, the number of AVR patients without revascularization in our region can be calculated to 110 per year. Considering the exclusion criteria as well as that some AVR patients are caused by aortic insufficiency, endocarditis, or a more acute course and that some patients are evaluated outside our institution, the number of potential eligible patients for the study may be estimated to not be higher than 140 to 160 in the two-year study period. Accordingly, it may be estimated that our study patients (n=42) and study + reference (n=42+36) patients present 25 to 30% and 50 to 55% of all potentially eligible patients, respectively. Our patients (study group + reference group) constituted ~15% of the patients in the Notion Study [15]. We have no reasons to believe that our patients were treated differently from contemporary usual care or that they had different outcomes.