

Supplementary table 1. Influence of age and LDLc on morphological and hemodynamic parameters of aortic valve in cases and controls.

Morphological and hemodynamic parameters	Controls				Cases			
	Per each 10 year Diff/OR (95% CI)	P-value	Per each 10 mg/dl of cLDL Diff/OR (95% CI)	P - value	Per each 10 year Diff/OR (95% CI)	P - value	Per each 10 mg/dl cLDL Diff/OR (95% CI)	P -value
Mean aortic valve pressure gradient (mm)	0.785 (-0.023, 1.592)	0.060	0.067 (-0.138, 0.272)	0.525	4.085 (2.077, 6.093)	<0.001	0.087 (-0.096, 0.269)	0.353
Maximum aortic velocity (Vmax) (m/s)	0.120 (0.003, 0.237)	0.048	0.014 (-0.016, 0.044)	0.365	0.341 (-0.143, 0.539)	0.001	0.012 (0.006, 0.030)	0.187
Aortic valve area (cm2)	-0.257 (-0.396, -0.117)	0.001	-0.024 (-0.059, 0.012)	0.189	-0.328 (-0.506, -0.150)	<0.001	-0.013(-0.029, 0.002)	0.099
Left ventricular ejection fraction (%)	2.569 (0.597, 4.541)	0.012	0.072 (-0.408, 0.552)	0.770	-2.515 (-5.203, 0.173)	0.069	0.012 (-0.231, 0.255)	0.923
Calcification of the aortic valve leaflets (score)	0.489 (0.249, 0.729)	<0.001	0.033 (-0.028, 0.094)	0.288	0.682(0.422, 0.941)	<0.001	0.026 (0.003, 0.049)	0.028
Valvular thickening >3 mm, % [n]	3.26 (1.31, 8.81)	0.013	1.18 (0.94, 1.54)	0.182	1.26 (0.66, 2.36)	0.463	1.03 (0.97, 1.09)	0.304
Aortic stenosis, % [n]	2.63 (1.13, 6.48)	0.027	0.97 (0.79, 1.22)	0.817	1.93 (0.98, 3.81)	0.054	1.04 (0.98, 1.11)	0.190
Aortic stenosis moderate or severe, % [n]	-		-		2.65 (1.01, 6.90)	0.041	1.02 (0.91, 1.13)	0.684
Aortic sclerosis, % [n]	1.95 (1.02, 3.92)	0.049	1.02 (0.87, 1.20)	0.797	1.30 (0.72, 2.40)	0.391	1.01 (0.96, 1.07)	0.691

Linear and logistic regressions based on generalized linear models (GLM) stratified by cases and controls. CI: Confidence Interval. P-value: adjusting for age and sex

Supplementary table 2. Baseline clinical and laboratory characteristics of HeFH with aortic valve conditions

Mean (SD) / proportion [n]		Normal valve		Aortic sclerosis		Aortic (mild)		Aortic stenosis (moderate or severe)	
	N	mean/%	N	mean/%	N	mean/%	N	mean/%	P -value
Age (years)	34	69.2 (3.9)	55	72.4 (6.3)	15	72.8 (6.5)	8	76.1 (12.0)	0.002
Sex, women % [n]	34	61.8 [21]	55	70.9 [39]	15	66.7 [10]	8	50 [4]	0.574
Systolic blood pressure (mmHg)	34	131.8 (15.2)	54	133.9 (16.2)	15	135.8 (19.2)	7	143.3 (25.4)	0.044
Diastolic blood pressure (mmHg)	34	77.7 (9.1)	54	76.6 (10.5)	15	78.5 (9.6)	7	74.6 (8.3)	0.993
Body mass index (Kg/m ²)	34	27.9 (3.5)	53	28.1 (4.2)	15	30.1 (4.7)	8	27.1 (2.9)	0.811
Tendon xanthomas, % [n]	30	26.7 [8]	50	42.0 [21]	14	42.9 [6]	8	62.5 [5]	0.027
Hypertension, % [n]	34	38.2 [13]	55	54.5 [30]	15	86.7 [13]	8	62.5 [5]	0.024
Type 2 Diabetes, % [n]	34	11.8 [4]	55	23.6 [13]	15	26.7 [4]	8	37.5 [3]	0.093
Previous cardiovascular disease, % [n]	34	17.6 [6]	55	30.9 [17]	15	33.3 [5]	8	37.5 [3]	0.300
Family history of premature cardiovascular disease, % [n]	31	32.3 [10]	52	46.2 [24]	13	69.2 [9]	4	50 [2]	0.036
Packages/day · years	33	10.3 (17.9)	53	8.4 (20.6)	15	11.8 (32.4)	7	12.7 (21.1)	0.880
Statin treatment (years)	34	22.4 (8.6)	53	22.9 (9.3)	15	22.5 (8.9)	8	20.9 (5.7)	0.906
Ezetimibe treatment, % [n]	34	79.4 [27]	55	81.8 [45]	15	86.7 [13]	8	100 [8]	0.281
Untreated total cholesterol (mg/dl)	33	380.7 (58.4)	55	398.7 (79.3)	15	416.4 (77.8)	8	401 (74.2)	0.119
Untreated triglycerides (mg/dl)	34	143.1 (78.4)	55	139.5 (81.9)	15	134.8 (62.4)	8	136.4 (60.2)	0.675
Untreated HDLc (mg/dl)	34	55.8 (13.9)	55	56.3 (13.9)	15	54.2 (12.9)	8	54.4 (13.3)	0.787
Untreated LDLc (mg/dl)	34	296.7 (59.6)	54	318.3 (76.5)	15	335.2 (76.7)	8	321.4 (68.6)	0.091
Lp(a) (mg/dl)	18	51.8 (54.1)	26	67.7 (71.6)	9	45.6 (46.1)	6	55.1 (45.4)	0.888

Continuous data presented as mean ± SD; categorical data presented as percentages. BP: blood pressure, BMI: body mass index, HDLc: high-density lipoprotein cholesterol, LDLc: low-density lipoprotein cholesterol. P -value from linear and logistic regressions based on generalized linear models (GLM), adjusted for age and sex