eTable 1a. Parsimonious Model: Incremental Risk Factors for Death in Isolated Aortic Stenosis Group

Risk Factor	Coefficient ± SE	P	Reliability (%)[a]
Early hazard phase			
Older age[b]	1.9 ± 0.51	.0001	75
NYHA functional class III/IV	0.88 ± 0.24	.0003	74
Lower HDL[c]	0.097 ± 0.036	.006	93
Higher creatinine[d]	-1.2 ± 0.43	.004	99
Higher bilirubin	0.25 ± 0.12	.04	63
Lower hematocrit[e]	-1.5 ± 0.51	.004	47
Lower LV diastolic volume[f]	0.10 ± 0.027	.0002	78
Late hazard phase			
Older age[b]	3.7 ± 0.44	<.0001	100
Larger BMI[g]	0.41 ± 0.11	.0003	68
Syncope	0.34 ± 0.14	.02	73
Smoking	0.25 ± 0.11	.02	74
COPD	0.59 ± 0.16	.0003	64
Higher BUN[h]	0.14 ± 0.036	.0002	98
Lower ejection fraction[i]	-0.63 ± 0.29	.03	96
Larger LA diameter[j]	0.86 ± 0.36	.02	89
LV mass index[k]	0.73 ± 0.18	<.0001	69
Interaction: age and LV mass index[l]	-0.66 ± 0.21	.002	

a. Percent of times variable appeared in 250 bootstrap models.

b. $(Age/75)^2$, squared transformation.

c. $(50/HDL)^2$, inverse squared transformation.

d. $(1/creatinine)$, inverse transformation.

e. $(Hematocrit/40)^2$, squared transformation.

f. $(100/LV\ diastolic\ volume)^2$, inverse squared transformation.

g. $(BMI/30)^2$, squared transformation.

h. $(BUN/20)^2$, squared transformation.

i. $(Ejection\ fraction/55)$, scaled variable.

j. $(LA\ diameter/4.5)$, scaled variable.

k. $(LV\ mass\ index/125)^2$, squared transformation.

l. Interaction: $(age/75)^2 \bullet (LV\ mass\ index/125)^2$.

Key: *AS,* aortic stenosis; *BMI,* body mass index; *BUN,* blood urea nitrogen; *COPD,* chronic obstructive pulmonary disease; *HDL,* high-density lipoprotein; *LA,* left atrial; *LV*, left ventricle; *NYHA,* New York Heart Association; *SE*, standard error.

eTable 1b. Parsimonious Model: Incremental Risk Factors for Death in Aortic

Stenosis+Coronary Artery Disease Group

Risk Factor	Coefficient ± SE	*P*	Reliability (%)[a]
Early hazard phase			
Older age[b]	2.01 ± 0.44	<.0001	88
Larger height/weight ratio	0.64 ± 0.19	.0007	73
NYHA functional class III/IV	0.58 ± 0.16	.0002	81
Aortic valve regurgitation 3+/4+	0.64 ± 0.036	.02	83
Tricuspid valve regurgitation 4+	1.04 ± 0.39	.007	80
Heart failure	0.39 ± 0.16	.02	50
Carotid disease (less risk)	-0.35 ± 0.15	.02	62
COPD	0.56 ± 0.18	.002	53
Treated diabetes	0.57 ± 0.17	.0006	76
Higher creatinine[c]	-0.69 ± 0.26	.008	96
Lower ejection fraction	0.061 ± 0.022	.006	86
Smaller AV prosthesis (Z-value)	-0.27 ± 0.086	.002	79
Earlier date of operation[d]	1.2 ± 0.39	.003	76
LMT stenosis ≥70%	0.72 ± 0.26	.005	96
LAD stenosis ≥70%	0.35 ± 0.16	.03	96
RCA stenosis ≥50%	0.43 ± 0.18	.02	96
LCx stenosis >0%	0.62 ± 0.27	.02	96
Late hazard phase			
Older age[b]	2.3 ± 0.24	<.0001	100
Insulin-treated diabetes	0.72 ± 0.13	<.0001	99
Smoking	0.26 ± 0.079	.001	87
Dialysis	1.4 ± 0.33	.0002	100
Higher BUN[e]	0.063 ± 0.015	<.0001	100

Lower hematocrit[f]	-0.69 ± 0.16	<.0001	78
Myocardial infarction	0.24 ± 0.084	.004	88
Lower ejection fraction[g]	-0.47 ± 0.18	.01	88
Larger LA diameter[h]	0.24 ± 0.43	.6	98
LV mass index[i]	-0.40 ± 0.22	.07	87
Interaction: LA diameter and LV mass index	0.46 ± 0.18	.01	
Atrial fibrillation surgical procedure	0.65 ± 0.20	.002	96
ASD/PFO suture closure	0.82 ± 0.33	.01	96
ITA used (less risk)	-0.24 ± 0.078	.002	96

a. Percent of times variable appeared in 250 bootstrap models.

b. $(Age/75)^2$, squared transformation.

c. (1/creatinine), inverse transformation.

d. (1/[interval to date of operation from 1/1/91]), inverse transformation.

e. $(BUN/20)^2$, squared transformation.

f. $(Hematocrit/40)^2$, squared transformation.

g. (Ejection fraction/55), scaled variable.

h. (LA diameter/4.5), scaled variable.

i. $(LV mass index/125)^2$, squared transformation.

j. Interaction: $(LA diameter/4.5) \cdot (LV mass index/125)^2$.

Key: *AS,* aortic stenosis; *ASD/PFO,* atrial septal defect/patent foramen ovale; *BUN,* blood urea nitrogen; *COPD,* chronic obstructive pulmonary disease; *ITA*, internal thoracic artery; *LA,* left atrial; *LAD,* left anterior descending coronary artery; *LCx,* left circumflex coronary artery; *LMT,* left main trunk; *LV*, left ventricle; *NYHA,* New York Heart Association; *RCA,* right coronary artery; *SE*, standard error.

eTable 1c. Semi-Saturated Models. Incremental Risk Factors for Death after Procedure (bolded entries represent statistically significant factors)

Risk Factor	Isolated AS		AS+CAD	
	Coefficient ± SE	*P*	Coefficient ± SE	*P*
Early hazard phase				
Older age[a]	**1.9 ± 0.55**	**.0007**	**1.9 ± 0.45**	**<.0001**
Larger height/weight ratio	0.30 ± 0.31	.3	**0.54 ± 0.20**	**.007**
NYHA functional class III/IV	**0.701 ± 0.25**	**.005**	**0.55 ± 0.16**	**.0004**
AV regurgitation 3+/4+	0.39 ± 0.42	.4	**0.64 ± 0.27**	**.02**
TV regurgitation 4+	0.33 ± 0.59	.6	**1.03 ± 0.39**	**.007**
Lower HDL[b]	0.072 ± 0.051	.2	-0.019 ± 0.036	.6
Carotid disease (less risk)	0.097 ± 0.24	.7	**-0.35 ± 0.15**	**.02**
COPD	0.48 ± 0.302	.11	**0.48 ± 0.18**	**.01**
Treated diabetes	0.52 ± 0.30	.08	**0.53 ± 0.17**	**.002**
Higher creatinine[c]	**-1.2 ± 0.45**	**.007**	**-0.65 ± 0.26**	**.01**
Higher bilirubin	0.23 ± 0.15	.13	0.070 ± 0.11	.5
Lower hematocrit[d]	**-1.3 ± 0.55**	**.02**	-0.65 ± 0.35	.06
Heart failure	0.36 ± 0.26	.17	**0.35 ± 0.17**	**.04**
Lower ejection fraction	0.020 ± 0.041	.6	0.062 ± 0.022	.007

Lower LV diastolic volume[e]	**0.11 ± 0.027**	**<.0001**	-0.0071 ± 0.049	.9
Smaller AV prosthesis (Z-value)	-0.037 ± 0.14	.8	**-0.25 ± 0.088**	**.004**
Earlier date of operation[f]	0.55 ± 0.65	.4	**1.3 ± 0.39**	**.001**
LMT stenosis ≥70%	—	—	**0.73 ± 0.25**	**.004**
LAD stenosis ≥70%	—	—	**0.36 ± 0.16**	**.03**
RCA stenosis ≥50%	—	—	**0.42 ± 0.18**	**.02**
LCx stenosis >0%	—	—	**0.63 ± 0.27**	**.02**
Late hazard phase				
Older age[a]	**3.6 ± 0.45**	**<.0001**	**2.1 ± 0.40**	**<.0001**
Larger BMI[g]	**0.42 ± 0.11**	**.0002**	-0.062 ± 0.13	.6
Syncope	**0.33 ± 0.14**	**.02**	0.20 ± 0.11	.06
Insulin-treated diabetes	0.11 ± 0.31	.7	**0.72 ± 0.13**	**<.0001**
Smoking	**0.29 ± 0.11**	**.01**	**0.26 ± 0.081**	**.002**
Dialysis	0.81 ± 0.65	.2	**1.4 ± 0.32**	**.0001**
Higher BUN[h]	**0.12 ± 0.037**	**.002**	**0.061 ± 0.015**	**<.0001**
Lower hematocrit[e]	-0.42 ± 0.26	.11	**-0.64 ± 0.16**	**.0001**
COPD	**0.58 ± 0.17**	**.0006**	0.12 ± 0.12	.3
Myocardial infarction	0.19 ± 0.18	.3	**0.24 ± 0.083**	**.004**
Lower ejection fraction[i]	**-0.56 ± 0.27**	**.04**	**-0.47 ± 0.18**	**.01**
Larger LA diameter[j]	0.84 ± 0.67	.2	0.26 ± 0.43	.6

LV mass index[k]	0.60 ± 0.51	.2	-0.54 ± 0.31	.09
Interaction: LA diameter and LV mass index[l]	0.08 ± 0.40	.8	**0.46 ± 0.18**	**.01**
Interaction: age and LV mass index[m]	**-0.61 ± 0.21**	**.004**	0.13 ± 0.22	.6
Atrial fibrillation surgical procedure	0.34 ± 0.41	.4	**0.66 ± 0.20**	**.001**
ASD/PFO suture closure	-0.16 ± 0.55	.8	**0.84 ± 0.26**	**.001**
ITA used (less risk)	—	—	**-0.24 ± 0.079**	**.002**

a. $(Age/75)^2$, squared transformation.

b. $(50/HDL)^2$, inverse squared transformation.

c. $(1/creatinine)$, inverse transformation.

d. $(Hematocrit/40)^2$, squared transformation.

e. $(100/LV\ diastolic\ volume)^2$, inverse squared transformation.

f. $(1/[interval\ to\ date\ of\ operation\ from\ 1/1/91])$, inverse transformation.

g. $(BMI/30)^2$, squared transformation.

h. $(BUN/20)^2$, squared transformation.

i. $(Ejection\ fraction/55)$, scaled variable.

j. $(LA\ diameter/4.5)$, scaled variable.

k. $(LV\ mass\ index/125)^2$, squared transformation.

l. Interaction: (LA diameter/4.5) • (LV mass index/125)^2.

m. Interaction: (age/75)^2 • (LV mass index/125)^2.

Key: *AS*, aortic stenosis; *ASD/PFO,* atrial septal defect/patent foramen ovale; *AV*, aortic valve; *BMI,* body mass index; *BUN,* blood urea nitrogen; *CAD*, coronary artery disease; *COPD,* chronic obstructive pulmonary disease; *HDL,* high-density lipoprotein; *ITA*, internal thoracic artery; *LA,* left atrial; *LAD,* left anterior descending coronary artery; *LCx,* left circumflex coronary artery; *LMT,* left main trunk; *LV*, left ventricle; *NYHA,* New York Heart Association; *RCA,* right coronary artery; *SE*, standard error; *TV*, tricuspid valve.

eTable 2. Postoperative Morbidity and Mortality before and after Matching

Variable	Before Matching			After Matching		
	Isolated AS (n=1,637)	AS+CAD (n=2,286)		Isolated AS (n=1,082)	AS+CAD (n=1,082)	
	No. (%)	No. (%)	*P*	No. (%)	No. (%)	*P*
Hospital death	21 (1.3)	55 (2.4)	.01	19 (1.8)	19 (1.8)	>.9
Myocardial infarction	4 (0.24)	10 (0.44)	.3	4 (0.31)	7 (0.65)	.4
Septicemia	26 (1.6)	63 (2.8)	.02	22 (2.0)	24 (2.2)	.8
Permanent stroke	25 (1.5)	53 (2.3)	.08	21 (1.9)	24 (2.2)	.6
Atrial fibrillation	531 (32)	829 (36)	.01	367 (34)	387 (36)	.4
Deep sternal wound infection	12 (0.73)	22 (0.96)	.4	9 (0.83)	6 (0.55)	.4
Reoperation for bleeding/tamponade	60 (3.7)	102 (4.5)	.2	41 (3.8)	51 (4.7)	.3
Cardiac reoperation excluding valve dysfunction or graft occlusion	19 (1.2)	25 (1.1)	.8	15 (1.4)	10 (0.92)	.3
Other noncardiac reoperation	19/1,101 (1.7)	37/1,344 (2.8)	.09	13/693 (1.9)	12/665 (1.8)	.9
Renal failure	58 (3.5)	146 (6.4)	<.0001	49 (4.5)	52 (4.8)	.8

Renal failure requiring dialysis	13 (0.79)	46 (2.0)	.002	12 (1.1)	16 (1.5)	.4
Prolonged ventilation (>24 h)	70/1,101 (6.4)	188/1,344 (14)	<.0001	46/693 (6.6)	72/665 (11)	.006
New permanent pacemaker	40/1,573 (2.5)	72/2,170 3.3	.17	28/1,024 2.7	33/1,037 3.2	.5

Key: *AS,* aortic stenosis; *CAD,* coronary artery disease.

eTable 3a. Unmatched vs. Matched Patient Characteristics of Patients with Isolated Severe Aortic Stenosis

Characteristic	Unmatched (n=555)		Matched (n=1,082)		
	n[a]	No. (%)	n[a]	No. (%)	*P*
Demography					
Female	555	319 (57)	1,082	450 (42)	<.0001
Age (years)	555	64 ± 11	1,082	73 ± 9.4	<.0001
BSA (m^2)	548	2.0 ± 0.30	1,059	2.0 ± 0.26	.9
Symptoms					
Preoperative NYHA functional class	548		1,059		<.0001
I		173 (32)		222 (21)	
II		277 (51)		558 (53)	
III		92 (17)		233 (22)	
IV		6 (1.1)		46 (4.3)	
Canadian Angina class	398		833		.4
0		171 (43)		366 (44)	
I		116 (29)		275 (33)	
II		97 (24)		163 (20)	
III		13 (3.3)		26 (3.1)	
IV		1 (0.25)		3 (0.36)	
Syncope	411	56 (14)	860	120 (14)	.9
Dyspnea on exertion	381	195 (51)	789	418 (53)	.6
Shortness of breath	381	236 (62)	788	451 (57)	.13
Paroxysmal nocturnal dyspnea	381	23 (6.0)	787	61 (7.8)	.3
Orthopnea	381	45 (12)	787	105 (13)	.5

Valve pathology

Pure aortic stenosis	549	425 (77)	1,054	778 (74)	.11
Mixed aortic stenosis/regurgitation	549	109 (29)	1,054	223 (21)	.5
Bicuspid aortic valve	555	361 (65)	1,082	298 (28)	<.0001
Mitral valve regurgitation severity	527		982		<.0001
None		333 (63)		478 (49)	
Mild		125 (24)		294 (30)	
Moderate		60 (11)		158 (16)	
Moderately severe		7 (1.3)		43 (4.4)	
Severe		2 (0.38)		9 (0.92)	
Tricuspid valve regurgitation severity	528		990		.03
None		377 (71)		643 (65)	
Mild		107 (20)		211 (21)	
Moderate		29 (5.5)		91 (9.2)	
Moderately severe		11 (2.1)		31 (3.1)	
Severe		4 (0.76)		14 (1.4)	

Cardiac comorbidity

Previous myocardial infarction	555	9 (1.6)	1,082	117 (11)	
Atrial fibrillation/flutter	501	24 (4.8)	957	90 (9.4)	.002
Complete heart block	501	7 (1.4)	951	55 (5.8)	<.0001
Ventricular arrhythmia	510	46 (9.0)	982	121 (12)	.06
Heart failure	555	73 (13)	1,082	257 (24)	<.0001

Noncardiac comorbidity

Peripheral arterial disease	555	8 (1.4)	1,082	57 (5.3)	.0002
Carotid disease	555	76 (14)	1,082	424 (39)	<.0001
Stroke	555	17 (3.1)	1,082	85 (7.9)	.0001

Hypertension	555	281 (51)	1,082	782 (72)	<.0001
Insulin-treated diabetes	545	6 (1.1)	1,055	55 (5.2)	<.0001
Pharmacologically treated diabetes	547	44 (8.0)	1,055	199 (19)	<.0001
BUN (mg·dL^{-1})	549	18 ± 6.9	1,057	21 ± 8.7	<.0001
Creatinine (mg·dL^{-1})	548	0.94 ± 0.39	1,058	1.08 ± 0.47	<.0001
Preoperative renal dialysis	479	3 (0.63)	898	9 (1)	.5
Chronic obstructive pulmonary disease	555	69 (12)	1,082	132 (12)	.9
Smoking	553	267 (48)	1,077	536 (50)	.6
Cholesterol (mg·dL^{-1})	453	195 ± 46	813	183 ± 44	<.0001
Triglycerides (mg·dL^{-1})	452	133 ± 77	810	132 ± 74	.9
HDL cholesterol (mg·dL^{-1})	453	58 ± 19	808	51 ± 16	<.0001
LDL cholesterol (mg·dL^{-1})	453	111 ± 40	807	106 ± 38	.04
Bilirubin (mg·dL^{-1})	529	0.63 ± 0.33	1,000	0.69 ± 0.52	.02
Hematocrit (%)	534	40 ± 5.2	1,017	38 ± 5.5	<.0001
Concomitant procedures					
Mitral valve repair	555	5 (0.9)	1,082	17 (1.6)	.3
Tricuspid valve repair	555	7 (1.3)	1,082	26 (2.4)	.12
Aortic endarterectomy	555	12 (2.2)	1,082	37 (3.4)	.2
Any atrial fibrillation procedure	555	23 (4.1)	1,082	74 (6.8)	.03
Septal myectomy	555	9 (1.6)	1,082	21 (1.9)	.6
ASD/PFO suture closure	555	11 (2.0)	1,082	16 (1.5)	.4
Aortic valve prosthesis					
Valve size (mm)	555		1,082		.2
19		77 (14)		163 (15)	
21		171 (31)		312 (29)	
23		179 (32)		353 (33)	

25		103 (18)		200 (18)	
27		18 (3.2)		50 (4.6)	
29		7 (1.3)		4 (0.37)	
Standardized size (Z-value)	546	-0.42 ± 1.01	1,059	-0.42 ± 0.99	>.9

a. Patients with data available.

Key: *AS,* aortic stenosis, *ASD/PFO,* atrial septal defect/patent foramen ovale, *BSA,* body surface area; *BUN,* blood urea nitrogen; *CAD,* coronary artery disease, *HDL,* high-density lipoprotein; *LAD,* left anterior descending coronary artery; *LCx,* left circumflex coronary artery; *LDL,* low-density lipoprotein; *LMT,* left main trunk; *NYHA,* New York Heart Association; *RCA,* right coronary artery; *SD*, standard deviation.

eTable 3b. Preoperative Echocardiographic Measurements of Unmatched vs. Matched

Patients with Isolated Severe Aortic Stenosis

Variable	Unmatched (n=555)		Matched (n=1,082)		
	n^a	Mean ± SD	n^a	Mean ± SD	*P*
Aortic valve hemodynamics					
Area (cm^2)	484	0.65 ± 0.14	942	0.65 ± 0.14	.3
Mean gradient (mmHg)	499	55 ± 16	969	50 ± 16	<.0001
Peak gradient (mmHg)	499	94 ± 25	975	84 ± 25	<.0001
LV geometry					
Morphology					
Posterior wall thickness (cm)	498	1.3 ± 0.23	932	1.3 ± 0.24	.005
Septal thickness (cm)	501	1.4 ± 0.30	939	1.5 ± 0.28	.0007
Mass index (g·m^{-2})	490	120 ± 41	908	132 ± 43	<.0001
End-diastolic diameter (cm)	501	4.5 ± 0.75	945	4.6 ± 0.82	.001
End-systolic diameter (cm)	492	2.8 ± 0.78	940	3.01 ± 0.86	<.0001
Function					
Ejection fraction (%)	522	57 ± 8.8	987	54 ± 11	<.0001
Left atrium					
Diameter (cm)	465	3.9 ± 0.73	887	4.2 ± 0.75	<.0001

a. Patients with data available.

Key: *AS,* aortic stenosis, *CAD,* coronary artery disease; *SD*, standard deviation.

eTable 4a. Unmatched vs. Matched Patient Characteristics of Patients with Severe Aortic Stenosis and Coronary Artery Disease

Variable	Unmatched (n=1,204)		Matched (n=1,082)		P
	n^a	No. (%)	n^a	No. (%)	
Demography					
Female	1,204	316 (26)	1,082	458 (42)	<.0001
Age (y)	1,204	77 ± 7.2	1,082	73 ± 8.6	<.0001
BSA (m^2)	1,197	2.0 ± 0.25	1,066	2.0 ± 0.26	.4
Symptoms					
Preoperative NYHA functional class	1,197		1,066		<.0001
I		119 (9.9)		227 (21)	
II		621 (52)		559 (52)	
III		334 (28)		239 (22)	
IV		123 (10)		41 (3.8)	
Canadian Angina class	1,064		882		<.0001
0		317 (30)		307 (35)	
I		239 (22)		230 (26)	
II		370 (35)		286 (32)	
III		109 (10)		53 (6.01)	
IV		29 (2.7)		6 (0.68)	
Syncope	1,032	141 (14)	860	130 (15)	.4
Dyspnea on exertion	971	487 (50)	800	410 (51)	.6
Shortness of breath	971	513 (53)	801	463 (58)	.04
Paroxysmal nocturnal dyspnea	971	102 (11)	800	69 (8.6)	.2
Orthopnea	971	120 (12)	801	111 (14)	.4

Valve pathology

Pure aortic stenosis	1,163	888 (76)	1,056	794 (75)	.5
Mixed aortic stenosis/regurgitation	1,163	243 (21)	1,056	225 (21)	.8
Bicuspid aortic valve	1,204	115 (9.6)	1,082	296 (27)	<.0001
Mitral valve regurgitation severity	1,119		977		<.0001
None		433 (39)		490 (50)	
Mild		350 (31)		287 (29)	
Moderate		222 (20)		150 (15)	
Moderately severe		92 (8.2)		41 (4.2)	
Severe		22 (2.0)		9 (0.92)	
Tricuspid valve regurgitation severity	1,115		980		.07
None		693 (62)		624 (64)	
Mild		243 (22)		219 (22)	
Moderate		133 (12)		87 (8.9)	
Moderately severe		32 (2.9)		42 (4.3)	
Severe		14 (1.3)		8 (0.82)	

Coronary artery disease

Number of systems diseased ≥50%	1,204		1,080		<.0001
0		32 (2.7)		73 (6.8)	
1		330 (27)		473 (44)	
2		423 (35)		322 (30)	
3		419 (35)		212 (20)	
LMT disease ≥50%	1,059	189 (18)	973	107 (11)	<.0001
LAD system disease ≥50%	1,187	915 (77)	1,062	709 (67)	<.0001
LCx system disease ≥50%	1,153	679 (59)	1,036	455 (44)	<.0001
RCA system disease ≥50%	1,204	839 (70)	1,082	589 (54)	<.0001

Cardiac comorbidity

Previous myocardial infarction	1,204	540 (45)	1,082	112 (10)	<.0001
Atrial fibrillation/flutter	1,082	125 (12)	927	79 (8.5)	.02
Complete heart block	1,076	64 (5.9)	926	51 (5.5)	.7
Ventricular arrhythmia	1,107	144 (13)	967	130 (13)	.8
Heart failure	1,204	443 (37)	1,082	248 (23)	<.0001

Noncardiac comorbidity

Peripheral arterial disease	1,204	213 (18)	1,082	65 (6.0)	<.0001
Carotid disease	1,204	785 (65)	1,082	430 (40)	<.0001
Stroke	1,204	143 (12)	1,082	78 (7.2)	.0002
Hypertension	1,204	1,013 (84)	1,082	798 (74)	<.0001
Insulin-treated diabetes	1,157	159 (14)	1,056	53 (5.0)	<.0001
Pharmacologically treated diabetes	1,160	381 (33)	1,059	201 (19)	<.0001
BUN (mg·dL^{-1})	1,187	25 ± 12	1,062	21 ± 9.6	<.0001
Creatinine (mg·dL^{-1})	1,182	1.2 ± 0.63	1,053	1.1 ± 0.51	<.0001
Preoperative renal dialysis	1,021	20 (2.0)	908	14 (1.5)	.5
Chronic obstructive pulmonary disease	1,204	178 (15)	1,082	149 (14)	.5
Smoking	1,189	718 (60)	1,077	529 (49)	<.0001
Cholesterol (mg·dL^{-1})	849	177 ± 47	834	186 ± 45	<.0001
Triglycerides (mg·dL^{-1})	839	136 ± 82	829	134 ± 77	.8
HDL cholesterol (mg·dL^{-1})	842	46 ± 15	830	51 ± 15	<.0001
LDL cholesterol (mg·dL^{-1})	836	103 ± 42	830	109 ± 40	.002
Bilirubin (mg·dL^{-1})	1,102	0.66 ± 0.4	1,000	0.69 ± 0.67	.5
Hematocrit (%)	1,114	37 ± 5.5	1,010	38 ± 5.5	<.0001

Concomitant procedures

Mitral valve repair	1,204	64 (5.3)	1,082	13 (1.2)	<.0001

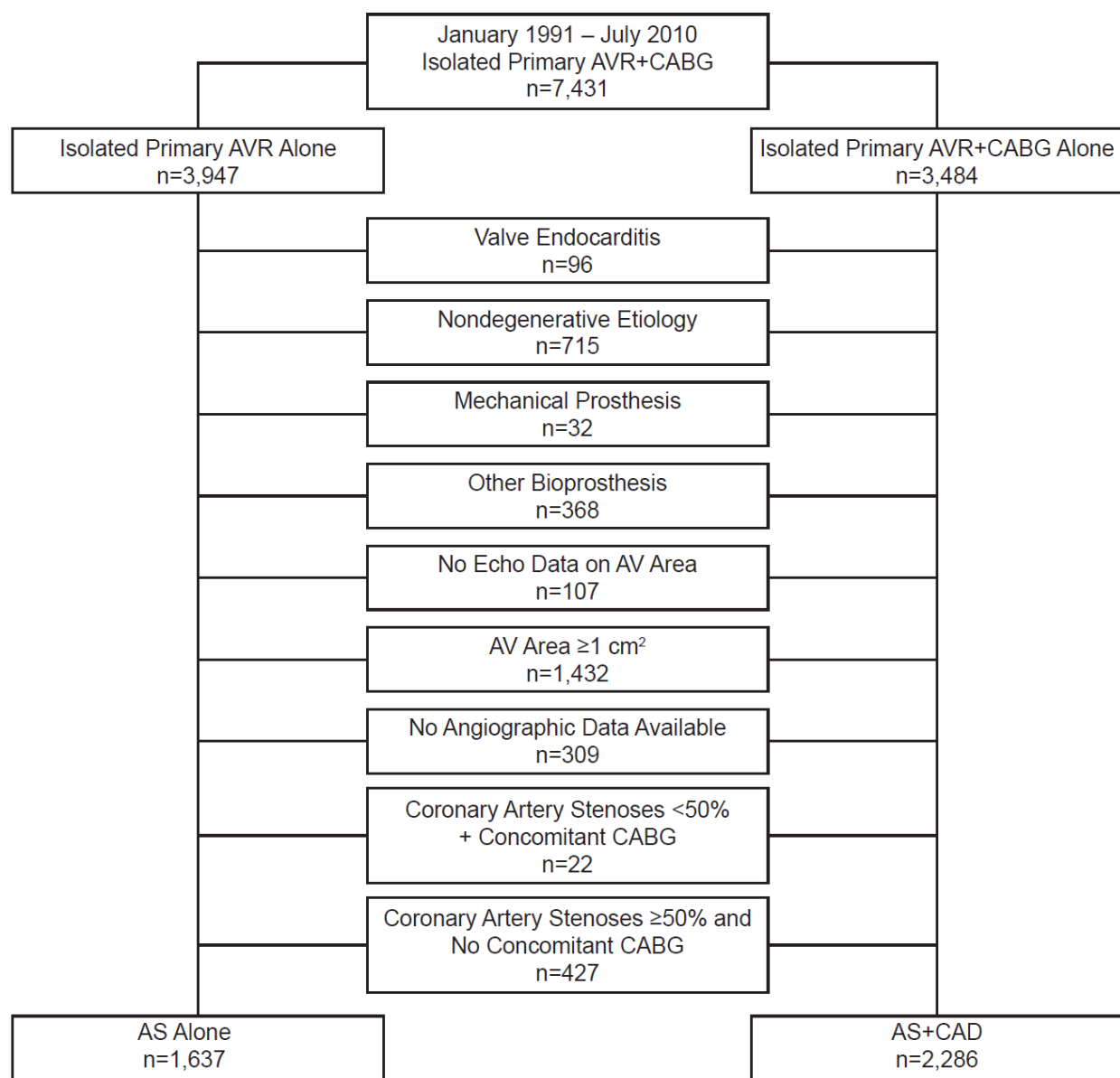|					
Tricuspid valve repair	1,204	26 (2.2)	1,082	27 (2.5)	.6
Aortic endarterectomy	1,204	85 (7.1)	1,082	40 (3.7)	.0004
Any atrial fibrillation procedure	1,204	72 (6.0)	1,082	71 (6.6)	.6
Septal myectomy	1,204	8 (0.66)	1,082	26 (2.4)	.0006
ASD/PFO suture closure	1,204	19 (1.6)	1,082	18 (1.7)	.9
Aortic valve prosthesis					
Valve size (mm)	1,204		1,082		<.0001
19		160 (13)		190 (18)	
21		347 (29)		319 (29)	
23		470 (39)		316 (29)	
25		187 (16)		207 (19)	
27		35 (2.9)		44 (4.1)	
29		5 (0.42)		6 (0.55)	
Standardized size (Z-value)	1,196	-0.4 ± 0.89	1,066	-0.42 ± 1.01	.5

a. Patients with data available.

Key: *AS,* aortic stenosis, *ASD/PFO,* atrial septal defect/patent foramen ovale, *BSA,* body surface area; *BUN,* blood urea nitrogen; *CAD,* coronary artery disease, *HDL,* high-density lipoprotein; *LAD,* left anterior descending coronary artery; *LCx,* left circumflex coronary artery; *LDL,* low-density lipoprotein; *LMT,* left main trunk; *NYHA,* New York Heart Association; *RCA,* right coronary artery; *SD*, standard deviation.

eTable 4b. Preoperative Echocardiographic Measurements in Unmatched vs. Matched Patients with Severe Aortic Stenosis and Coronary Artery Disease

Variable	Unmatched (n=1,204)		Matched (n=1,082)		
	n^a	Mean ± SD	n^a	Mean ± SD	*P*
Aortic valve hemodynamics					
Area (cm^2)	1,060	0.69 ± 0.15	932	0.66 ± 0.14	<.0001
Mean gradient (mmHg)	1,085	41 ± 15	957	49 ± 16	<.0001
Peak gradient (mmHg)	1,086	69 ± 24	956	84 ± 24	<.0001
LV geometry					
Morphology					
Posterior wall thickness (cm)	989	1.3 ± 0.24	905	1.3 ± 0.22	.4
Septal thickness (cm)	1,000	1.5 ± 0.32	915	1.5 ± 0.29	.06
Mass index (g·m^{-2})	977	137 ± 40	886	131 ± 42	.0002
End-diastolic diameter (cm)	1,007	4.8 ± 0.80	927	4.6 ± 0.82	<.0001
End-systolic diameter (cm)	991	3.2 ± 0.93	920	3.0 ± 0.85	<.0001
Function					
Ejection fraction (%)	1,128	48 ± 13	1,006	54 ± 11	<.0001
Left atrium					
Diameter (cm)	979	4.4 ± 0.75	857	4.2 ± 0.75	<.0001

a. Patients with data available.

Key: *CAD,* coronary artery disease; *SD*, standard deviation.

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                    ┌──────────────────────────────┐
                    │   January 1991 – July 2010   │
                    │  Isolated Primary AVR+CABG   │
                    │          n=7,431             │
                    └──────────────────────────────┘
   ┌─────────────────────────┐                   ┌──────────────────────────────┐
   │ Isolated Primary AVR    │                   │ Isolated Primary AVR+CABG    │
   │        Alone            │                   │         Alone                │
   │       n=3,947           │                   │        n=3,484               │
   └─────────────────────────┘                   └──────────────────────────────┘
                    ┌──────────────────────────────┐
                    │      Valve Endocarditis       │
                    │           n=96                │
                    └──────────────────────────────┘
                    ┌──────────────────────────────┐
                    │   Nondegenerative Etiology    │
                    │           n=715               │
                    └──────────────────────────────┘
                    ┌──────────────────────────────┐
                    │    Mechanical Prosthesis      │
                    │           n=32                │
                    └──────────────────────────────┘
                    ┌──────────────────────────────┐
                    │     Other Bioprosthesis       │
                    │           n=368               │
                    └──────────────────────────────┘
                    ┌──────────────────────────────┐
                    │    No Echo Data on AV Area    │
                    │           n=107               │
                    └──────────────────────────────┘
                    ┌──────────────────────────────┐
                    │       AV Area ≥1 cm²          │
                    │          n=1,432              │
                    └──────────────────────────────┘
                    ┌──────────────────────────────┐
                    │  No Angiographic Data Available│
                    │           n=309               │
                    └──────────────────────────────┘
                    ┌──────────────────────────────┐
                    │  Coronary Artery Stenoses <50%│
                    │      + Concomitant CABG       │
                    │           n=22                │
                    └──────────────────────────────┘
                    ┌──────────────────────────────┐
                    │ Coronary Artery Stenoses ≥50% and│
                    │     No Concomitant CABG       │
                    │           n=427               │
                    └──────────────────────────────┘
   ┌─────────────────────────┐                   ┌──────────────────────────────┐
   │       AS Alone          │                   │          AS+CAD              │
   │       n=1,637           │                   │         n=2,286              │
   └─────────────────────────┘                   └──────────────────────────────┘
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AV Area ≥1 cm^2

eFigure 1. CONSORT-style diagram depicting how study groups were formed from the entire

cohort of 7,431 patients.
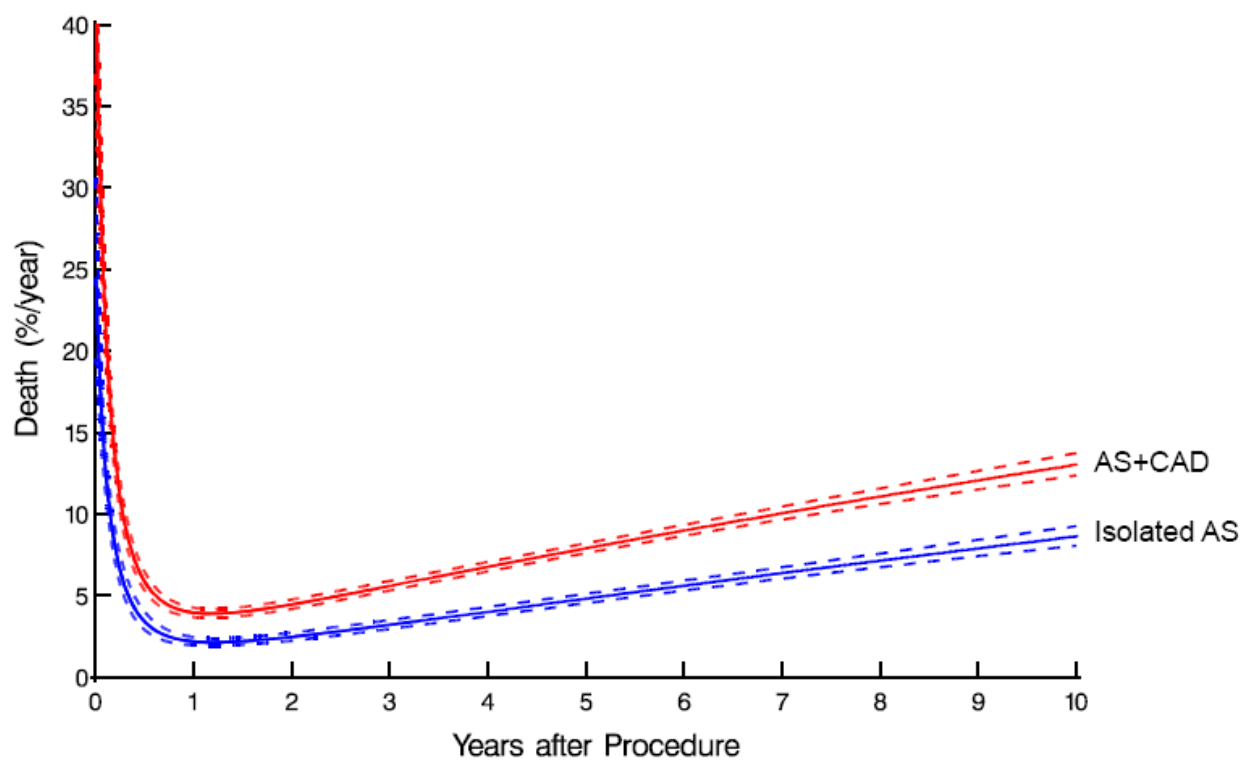
eFigure 2. Unadjusted instantaneous risk of death (hazard function) among patients with isolated aortic stenosis (blue; Isolated AS) vs. aortic stenosis with coronary artery disease (red; AS+CAD).

A, Instantaneous risk of death. Solid lines represent parametric estimates enclosed within asymmetric confidence bands equivalent to ±1 standard error.
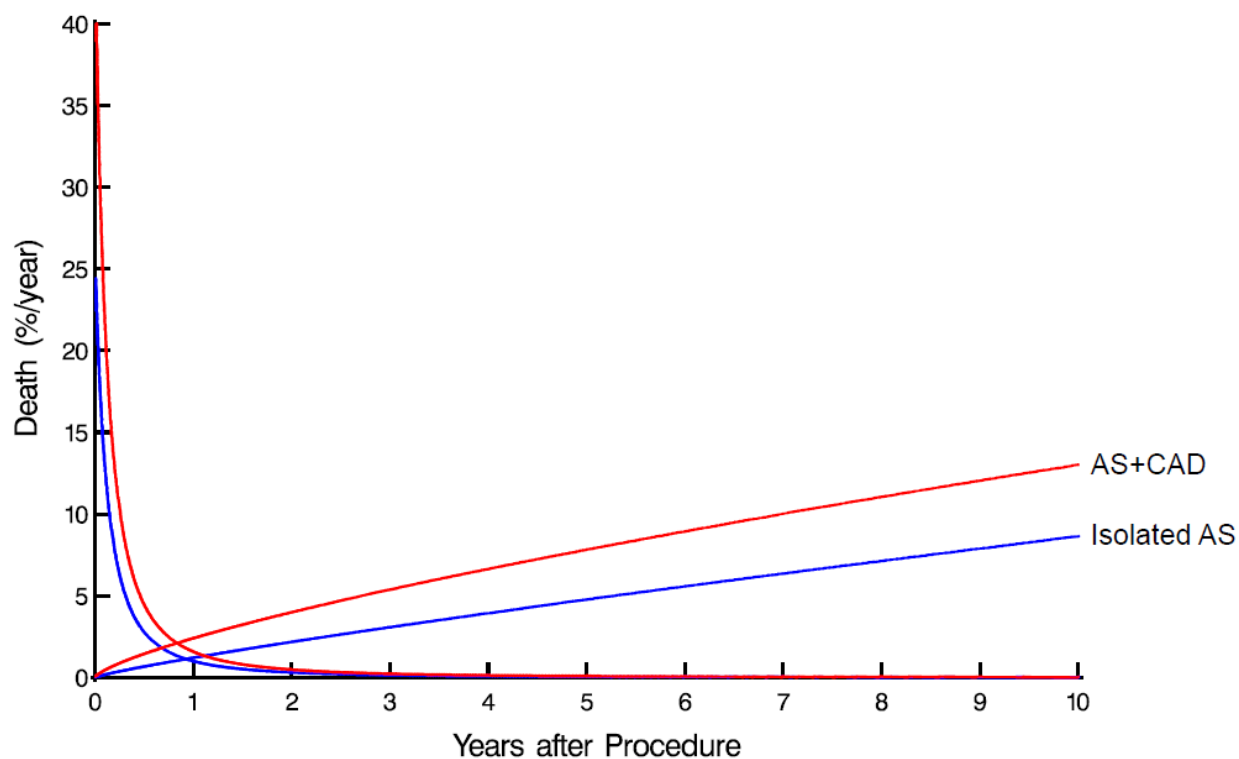
eFigure 2. Unadjusted instantaneous risk of death (hazard function) among patients with isolated aortic stenosis (blue; Isolated AS) vs. aortic stenosis with coronary artery disease (red; AS+CAD).

B, Components of the temporal decomposition of hazard that constitute *early* declining phase of risk and the *late* rising phase of risk.
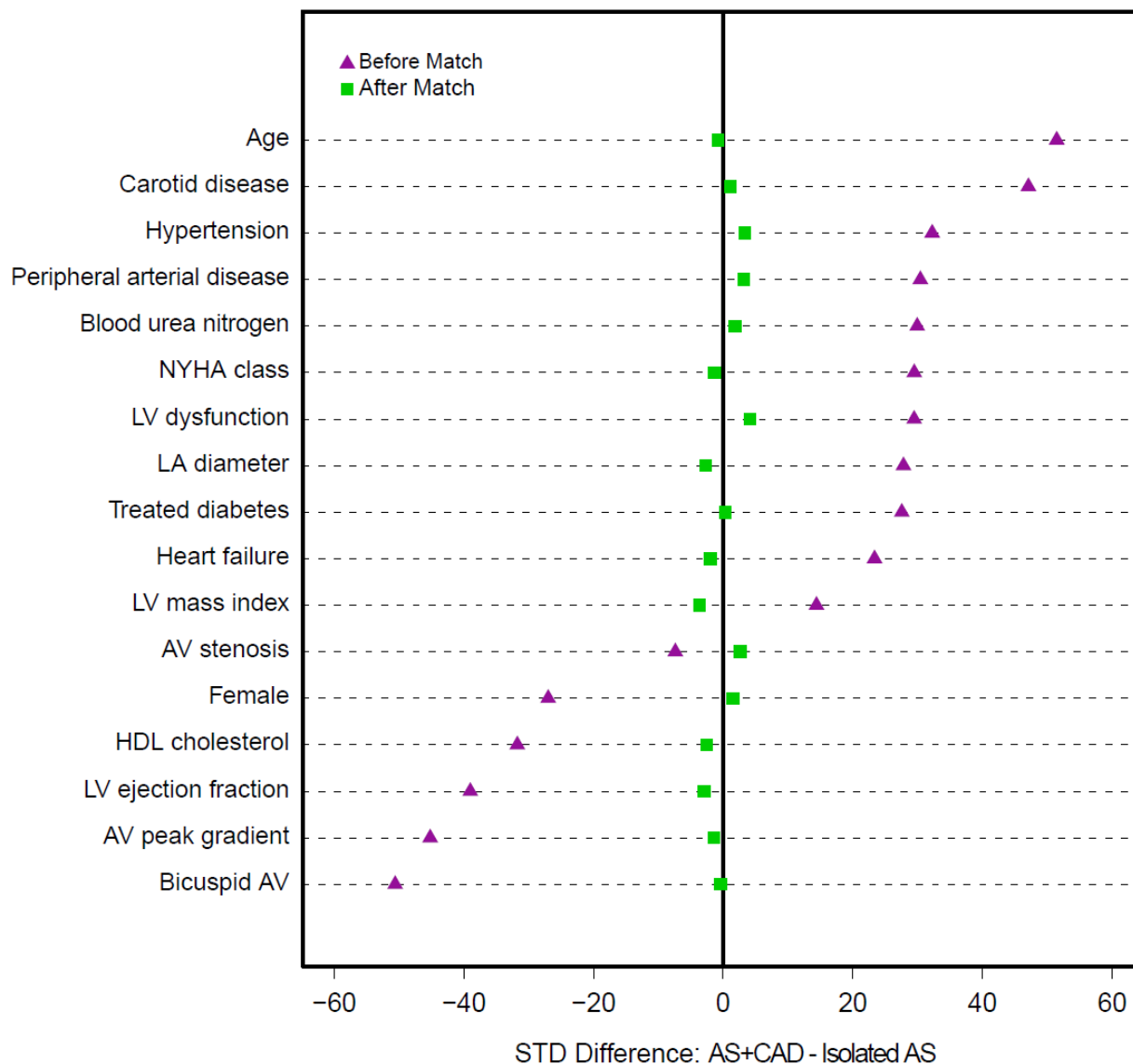
eFigure 3. Covariable balance for selected variables using standardized differences (STD) between patients with isolated severe aortic stenosis (AS) and those with coronary artery disease (AS+CAD) before (purple trianges) and after (green squares) matching (1). Key: *AV,* aortic valve; *HDL,* high-density lipoprotein; *LA,* left atrial; *LV,* left ventricular; *NYHA,* New York Heart Association.

1. Austin PC, Mamdani MM. A comparison of propensity score methods: a case study estimating the effectiveness of post-AMI statin use. Stat Med 2006;25:2084-106.
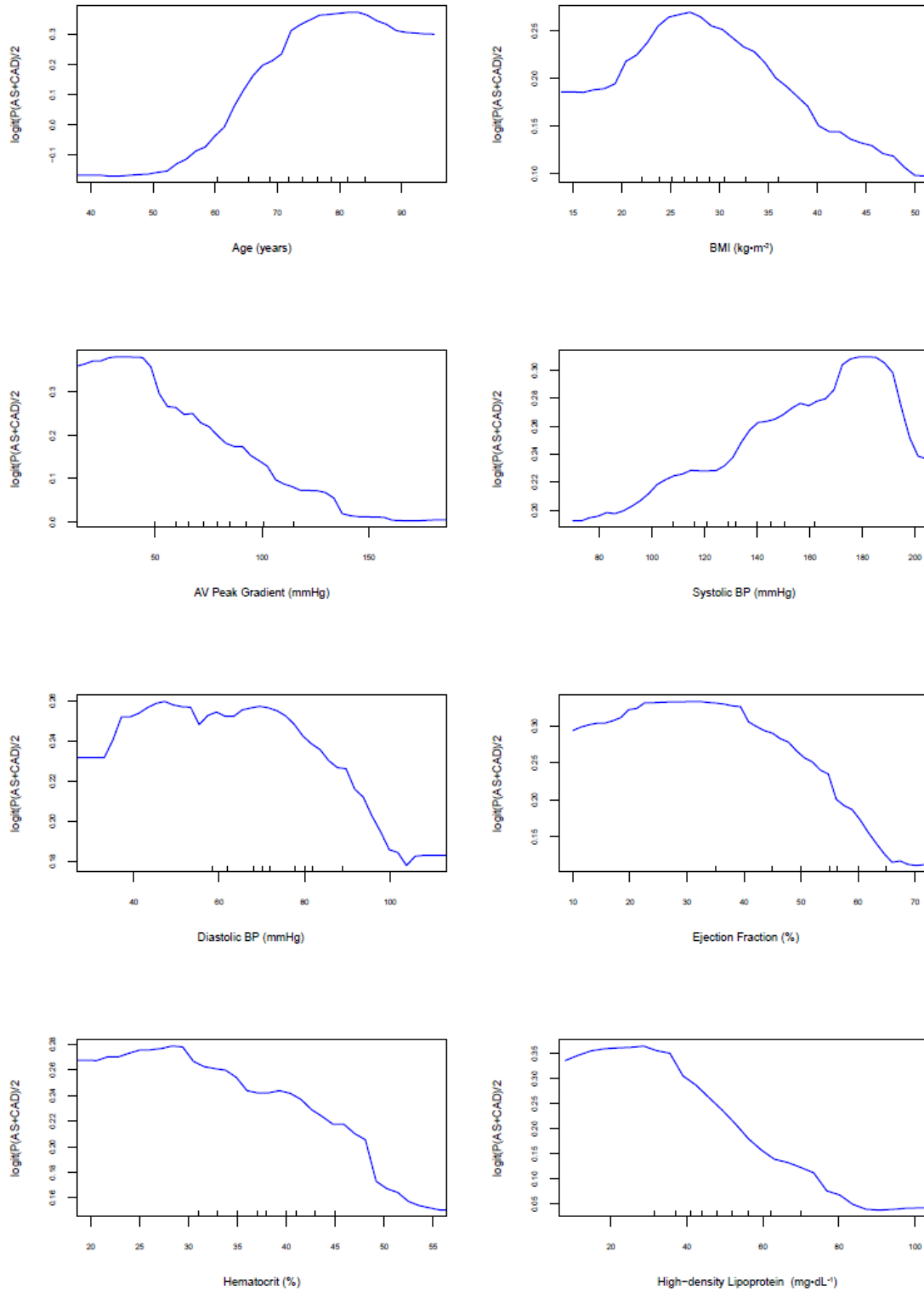
eFigure 4. Partial dependence plot for selected predictor variables (see Table 3) from random

forest prediction (eAppendix 2) of belonging to the aortic stenosis plus coronary artery disease

(AS+CAD) group. Partial dependence (vertical axis) is depicted as probability of being in the AS+CAD group for different values of the variable depicted along the horizontal axis after averaging out the effect of other variables in the model. Hash marks at the bottom of horizontal axis indicate the decile values of the variable being depicted.
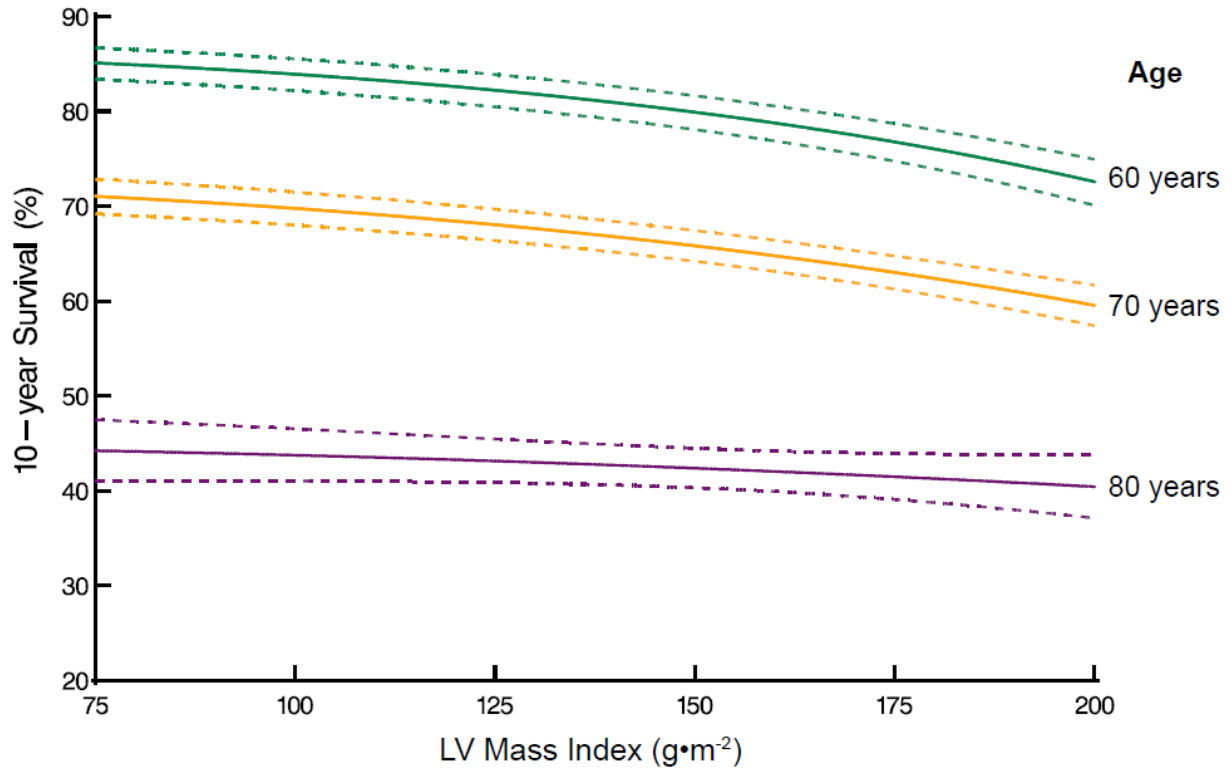
eFigure 5. Nomograms depicting 10-year survival after aortic valve replacement, illustrating

interactions observed in Table 4.

A, Illustration of interaction effect of age and LV mass index.
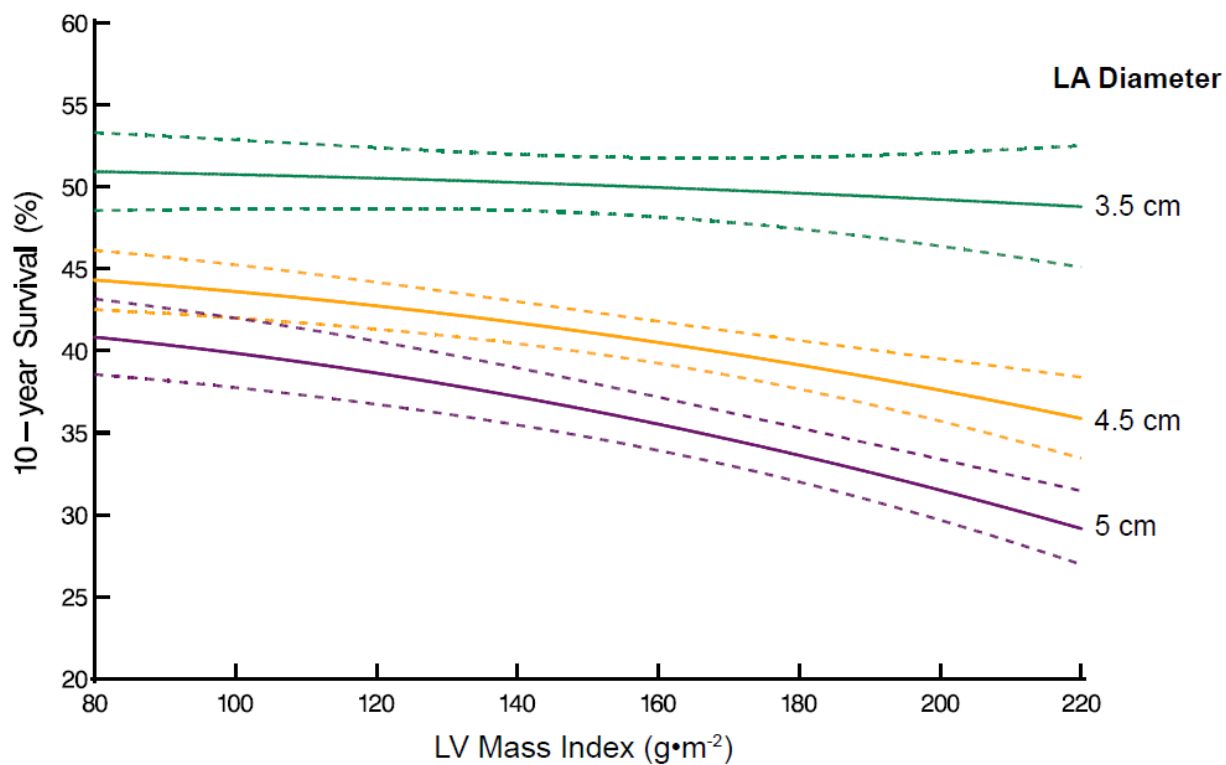
eFigure 5. Nomograms depicting 10-year survival after aortic valve replacement, illustrating interactions observed in Table 4.

B, Illustration of interaction effect: age, LV mass index, and left atrial (LA) diameter.
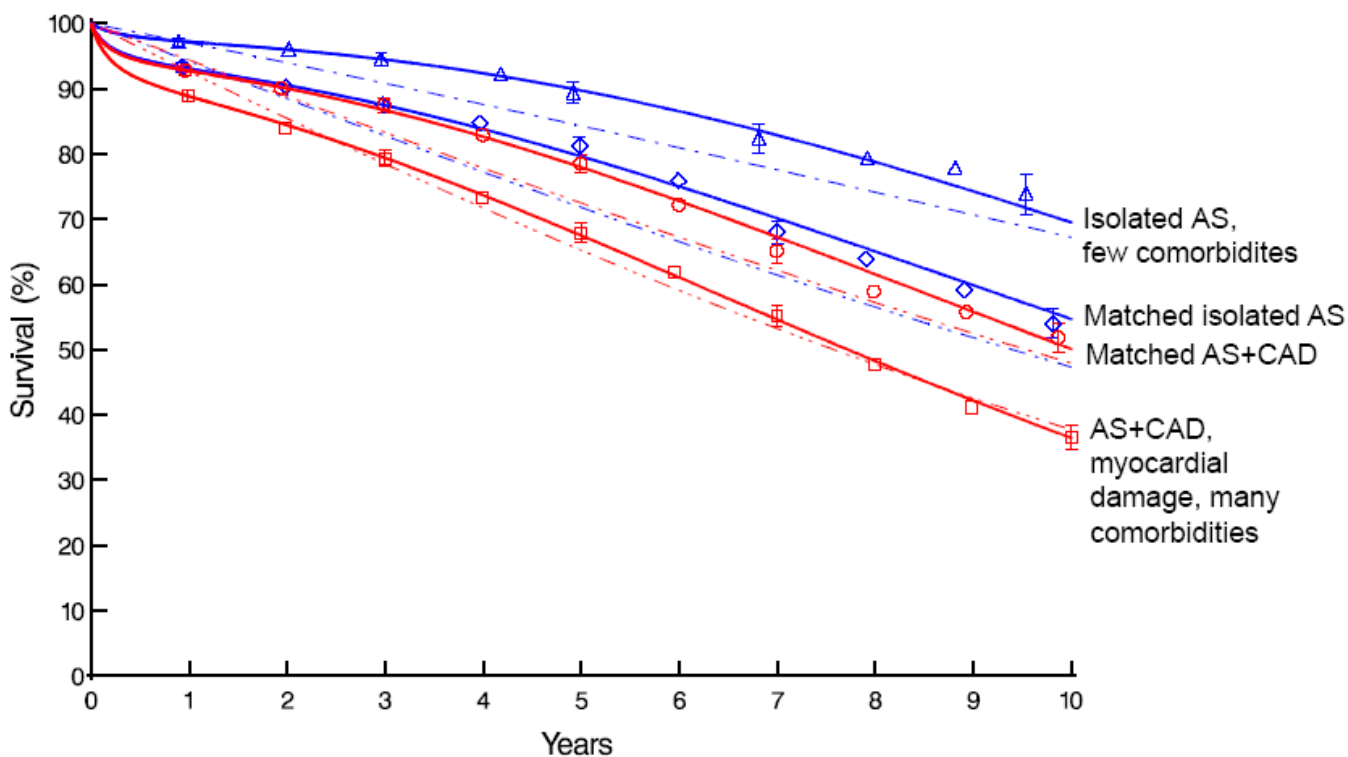
eFigure 6. Survival after aortic valve replacement (AVR) for patients with isolated severe aortic stenosis (AS) in the matched vs. unmatched subgroups referenced to age-sex-race–matched survival of the U.S. population. Each symbol represents a death, with vertical bars representing confidence limits equivalent to ±1 standard error. Red curves with open circles and open squares represent patients with AS plus coronary artery disease (AS+CAD), matched and unmatched, respectively. Blue curves with open triangles and open diamonds represent isolated AS patients, each with their respective matched and unmatched curves. Dot-dash lines are U.S. life table age-sex-race–matched survival curves for each subgroup.

eAppendix 1. Variables Used in Analyses

<u>**Patient**</u>

Demographic

Age (y)[*], gender[*], race*, weight (kg), height (cm), body surface area (m^2), body mass index

(kg•m^{-2})[*]

Symptoms

New York Heart Association functional class (I-IV)[*], Canadian angina class, emergency

operation, syncope*, dyspnea on exertion*, dyspnea at rest[*], paroxysmal nocturnal dyspnea*,

orthopnea*

Ventricular dysfunction

Previous myocardial infarction*, degree of left ventricular dysfunction (1=none, 2=mild,

3=moderate, 4=moderately severe, 5=severe)

Aortic valve pathophysiology

Aortic valve stenosis, mixed aortic stenosis and regurgitation, bicuspid valve[*], orifice area

(cm^2)*, mean gradient (mmHg)*, peak gradient (mmHg)[*]

Other functional valve pathophysiology

Mitral regurgitation*, mitral stenosis*, tricuspid regurgitation[*]

Coronary artery disease

Left main trunk stenosis (>0%, ≥50%), left anterior descending coronary artery stenosis (>0%,

≥50%), left circumflex coronary artery stenosis (>0%, ≥50%), right circumflex coronary artery

stenosis (>0%, ≥50%)

Left atrium

Left atrial diameter (cm)*, volume (mL), volume index (mL•m^{-2})

Left ventricle

Morphology: Inner diameter in diastole (cm), diastolic volume (mL), diastolic volume index

(mL•m^{-2})*, inner diameter in systole (cm), systolic volume (mL), systolic volume index

(mL•m^{-2}), posterior wall thickness (cm), septal thickness (cm), relative wall thickness (wall

stress), mass (g), mass index (g•m^{-2})*

Function: Ejection fraction (%)*, fractional shortening

Other cardiac comorbidity

Heart failure*, hypertension*, systolic blood pressure (mmHg)*, diastolic blood pressure

(mmHg)*, complete heart block/pacer*, atrial fibrillation*, ventricular arrhythmia*

Noncardiac comorbidity

Treated diabetes*, insulin-treated diabetes, peripheral arterial disease*, smoking, carotid disease,*

stroke*, chronic obstructive pulmonary disease*, creatinine (mg·dL^{-1}), creatinine clearance,

blood urea nitrogen (mg·dL^{-1})*, bilirubin (mg·dL^{-1})*, hematocrit (%)*, total cholesterol (mg·dL^{-1}

), high-density lipoprotein (mg·dL^{-1})*, low-density lipoprotein (mg·dL^{-1})*, triglycerides (mg·dL^{-1}

)*

Procedure

AV Prosthesis: Valve size, in-vitro effective orifice area (EOA), Z-value*, Z-value for EOA,

ratio: valve area/body surface area, ratio: EOA/body surface area, internal valve area, efficiency:

EOA/internal area

Concomitant Operation: Mitral valve repair or replacement*, tricuspid valve repair or replacement*, aortic endarterectomy[*], septal myectomy*, atrial septal defect/patent foramen ovale suture closure*, internal thoracic artery used for coronary artery bypass grafting,[b] surgery for atrial fibrillation*

Experience

Date of operation (years since 1/1/1991)

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Note: Asterisks indicate variables used for matching in propensity analysis.

a. Because of the group definition, only variables with stenosis >0% were considered in the aortic valve replacement group analyses.

b. Variable considered only in AS+CAD group.

eAppendix 2: Partial Dependence Plots Using Random Forest Classification

We used random forests (RF) classification (42) to identify and depict relationships between selected baseline variables and the likelihood of being in the AS+CAD group. The classification tree method constructs a tree by recursive binary partitioning into regions that are increasingly homogeneous with respect to AS+CAD. However, Breiman (42) demonstrated that classification accuracy can be improved substantially by aggregating results of many trees, each grown from a "bootstrap" dataset formed by randomly sampling the data with replacement to build a dataset of equal size to the original. About two-thirds of patients are unique in each sample and one-third duplicates. We used 1,000 trees for RF classification modeling using the variables listed in eAppendix 1, with 20 variables available for splitting at each node. We implemented the RF using "randomForest" package in R software (43). We prefer the RF approach when we want to depict the relationship (linear or nonlinear) between predictor and outcome variables because splits of continuous variables can occur at any set of values for each tree; by aggregating over a forest of trees, a near-continuous depiction can be obtained with no modeling assumptions (nonparametric).