

SUPPLEMENTAL MATERIAL

METHODS

Data collection and variable definitions

Patients' clinical and echocardiography data were collected at the time of mitral valve (MV) surgery. Hypertension was defined by one of the following: a previous diagnosis of hypertension, systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg, or the current use of antihypertensive medications. Diabetes mellitus was defined as either the previous diagnosis, fasting glucose ≥ 126 mg/mL or glycated hemoglobin $\geq 6.5\%$, or the current use of antihyperglycemic agents. Atrial fibrillation (AF) was defined as a previous diagnosis or documented AF or atrial flutter rhythm on the 12-lead electrocardiography. Stroke included both ischemic and hemorrhagic cerebrovascular events. Myocardial infarction was determined based on electrocardiography findings, elevated cardiac enzymes, and invasive coronary angiography results. Symptom status was collected at the time of MV surgery from the medical records. The type of mitral regurgitation (MR) surgery was categorized as MV repair or MV replacement with either mechanical valve or bioprosthetic valve based on the surgical records. Information on concomitant coronary artery bypass grafting or surgical atrial ablation was also collected.

Echocardiography

The left ventricle (LV) and left atrial (LA) dimensions were measured from the standard parasternal windows. The LV end-diastolic and end-systolic volumes were calculated from the apical 2-chamber and 4-chamber views, and LV ejection fraction was estimated by the biplane Simpson's method. The LV mass was calculated using the Devereux cube formula and indexed to body surface area. The peak E-velocity was acquired from the apical 4-chamber view. The tissue Doppler velocities were obtained at the medial side of the mitral

annulus. Tricuspid regurgitation (TR) peak velocity was obtained from the right ventricle-focused apical 4-chamber view.

Imputation method

Our database has a minimal proportion of missing values (**online supplemental figure 1**).

We used the *missForest* algorithm for the imputation, which uses a random forest model to predict missing values iteratively.¹ The *missForest* can deal with large-scale, mixed-type data including both categorical and continuous variables.¹ The number of decision trees for the *missForest* was set as 100, and 3 random variables were sampled at each split. The normalized root mean squared error and the proportion of falsely classified entries were 25.3% and 0.0% for continuous and categorical variables, respectively. In addition, as a sensitivity analysis, we performed LCA after excluding patients with any missing values (n=50 excluded). The result was almost identical to the LCA using the imputed dataset.

Internal validation analysis

For the internal validation, we performed multinomial logistic regression analysis with 100 bootstrap samples, where the dependent variable is the phenogroup membership (1 to 5), and the independent variables are the variables used for LCA. A multinomial logistic regression model was developed using the randomly selected 70% of the derivation cohort. The remaining 30% of the samples were used for validation of the model using various performance metrics (accuracy, F1-score, and area under the curve of the receiver operating characteristic curve). The distribution of these metrics from 100 iterations was estimated.²

Assignment of group membership in the validation cohort

Each patient in the validation cohort was assigned to the phenogroup according to the highest

probabilities of belonging, which was calculated from the partial probabilities of each variable (**online supplemental table 7**). Suppose patient A has the following characteristics:

	Patient A	Categories			
		1	2	3	4
Age	68 years	<50	50–60	<u>60–70</u>	≥70
Sex	men	<u>men</u>	women		
BMI	23 kg/m ²	<u>≤25</u>	≥25		
Hypertension	No	<u>No</u>	Yes		
Diabetes	Yes	No	<u>Yes</u>		
AF	Yes	No	<u>Yes</u>		
Symptoms	Yes	No	<u>Yes</u>		
Anemia ^a	No	<u>No</u>	Yes		
eGFR	57 mL/min/ 1.73m ²	≥90	90–60	<u>60–30</u>	<30
MV surgery	MV repair	<u>MV repair</u>	MVR mechanical	MVR bioprosthetic	
CABG	Yes	No	<u>Yes</u>		
LVESD	45 mm	<40	<u>≥40</u>		
LVEF	62%	<u>≥60</u>	≤60		
LA dimension	57 mm	<55	<u>≥55</u>		
TR velocity	3.3 m/s	≤2.8	<u>>2.8</u>		

^amen, hemoglobin <13g/dL; women, hemoglobin <12g/dL.

AF, atrial fibrillation; BMI, body mass index; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrium; LVEF, left ventricular ejection fraction;

LVESD, left ventricular end-systolic diameter; MV, mitral valve; MVR, mitral valve replacement; TR, tricuspid regurgitation

The probabilities of patient A belonging to group 1 is calculated by multiplying the partial probabilities of group 1 for each category (**online supplemental table 7**):

Group 1 probability = $0.028492 \text{ (Age)} \times 0.703620 \text{ (Sex)} \times 0.608755 \text{ (BMI)} \times 0.796451 \text{ (Hypertension)} \times 0.012656 \text{ (Diabetes)} \times 0.100215 \text{ (AF)} \times 0.197978 \text{ (Symptoms)} \times 0.852485 \text{ (Anemia)} \times 0.004756 \text{ (eGFR)} \times 0.979446 \text{ (MV surgery)} \times 1.18 \times 10^{-251} \text{ (CABG)} \times 0.292662 \text{ (LVESD)} \times 0.865954 \text{ (LVEF)} \times 0.06306 \text{ (LA dimension)} \times 0.206127 \text{ (TR velocity)} = 3.76 \times 10^{-262}$

Probabilities of group 2 to 5 can also be calculated using the same method:

Group 2 probability = 3.22×10^{-7}

Group 3 probability = 6.73×10^{-10}

Group 4 probability = 1.81×10^{-8}

Group 5 probability = 5.40×10^{-6}

Total sum of the probabilities = Group 1 probability + Group 2 probability + Group 3 probability + Group 4 probability + Group 5 probability = 5.74×10^{-6}

Final probability of group membership:

Group 1: $3.76 \times 10^{-262} / 5.74 \times 10^{-6} = 0.000$

Group 2: $3.22 \times 10^{-7} / 5.74 \times 10^{-6} = 0.056$

Group 3: $6.73 \times 10^{-10} / 5.74 \times 10^{-6} = 0.000$

Group 4: $1.81 \times 10^{-8} / 5.74 \times 10^{-6} = 0.003$

Group 5: $5.40 \times 10^{-6} / 5.74 \times 10^{-6} = 0.941$

Therefore, patient A is assigned to group 5 (*high-risk older patients*), the phenogroup with the maximal probabilities.

Reference for the online supplemental methods

1. Stekhoven DJ, Bühlmann P. MissForest--non-parametric missing value imputation for mixed-type data. *Bioinformatics* 2012;28:112-8.
2. Shah RV, Yeri AS, Murthy VL, Massaro JM, D'Agostino R Sr., Freedman JE, et al. Association of Multiorgan Computed Tomographic Phenomap With Adverse Cardiovascular Health Outcomes: The Framingham Heart Study. *JAMA Cardiol* 2017;2:1236-1246.

Supplemental Table 1. Variables used for the latent class analysis and their categorization.

Variables	Categories			
	1	2	3	4
Age, years	<50	50–60	60–70	≥70
Sex	men	women		
Body mass index, kg/m ²	<25	≥25		
Hypertension	No	Yes		
Diabetes	No	Yes		
Atrial fibrillation	No	Yes		
Symptoms	No	Yes		
Anemia ^a	No	Yes		
eGFR, mL/min/1.73m ²	≥90	90–60	60–30	<30
MV surgery type	MV repair	MV replace (mechanical)	MV replace (bioprosthetic)	
Concomitant CABG	No	Yes		
LV end-systolic diameter, mm	<40	≥40		
LV ejection fraction, %	>60	≤60		
LA dimension, mm	<55	≥55		
TR peak velocity, m/s	≤2.8	>2.8		

^amen, hemoglobin <13g/dL; women, hemoglobin <12g/dL.

CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrium; LV, left ventricle; MV, mitral valve; TR, tricuspid regurgitation.

Supplemental Table 2. Univariable Cox analysis for all-cause mortality after MV surgery in the derivation cohort.

Variables	All-cause mortality	
	HR (95% CI)	P
Age, year	1.07 (1.06-1.09)	<0.001
Male	0.65 (0.47-0.90)	0.010
Body mass index, kg/m ²	0.95 (0.91-0.99)	0.031
Hypertension	1.62 (1.17-2.23)	0.004
Diabetes	3.02 (2.00-4.56)	<0.001
Atrial fibrillation	2.37 (1.71-3.28)	<0.001
Stroke	0.41 (0.06-2.91)	0.371
Myocardial infarction	1.82 (0.67-4.92)	0.238
Year of MV surgery (2014–2020 vs. 2006-2013)	0.72 (0.46-1.13)	0.156
Symptomatic MR	1.53 (1.11-2.12)	0.010
Hemoglobin, g/dL	0.69 (0.64-0.75)	<0.001
eGFR, 10 mL/min/1.73m ²	0.77 (0.72-0.81)	<0.001
MR etiology		
Degenerative	1 (reference)	-
Rheumatic	1.34 (0.90-1.98)	0.146
Congenital	1.22 (0.30-4.96)	0.777
MR surgery type		
MV repair	1 (reference)	-
MV replacement (mechanical)	2.39 (1.61-3.55)	<0.001

MV replacement (bioprosthetic)	5.28 (3.43-8.13)	<0.001
Concomitant CABG	2.92 (1.90-4.50)	<0.001
Concomitant surgical atrial ablation	1.77 (1.28-2.44)	<0.001
LV end-systolic diameter, mm	1.03 (1.00-1.05)	0.022
LV end-diastolic diameter, mm	0.99 (0.97-1.02)	0.548
LV end-systolic volume, 10 mL	1.06 (1.00-1.12)	0.040
LV end-diastolic volume, 10 mL	0.97 (0.94-1.00)	0.082
LV end-systolic volume index, 10 mL/m ²	1.18 (1.09-1.28)	<0.001
LV end-diastolic volume index, 10 mL/m ²	1.00 (0.95-1.06)	0.982
LV ejection fraction, %	0.95 (0.93-0.97)	<0.001
LV mass index, 10 g/m ²	1.03 (1.01-1.06)	0.010
LA dimension, mm	1.03 (1.02-1.04)	<0.001
E-wave, m/s	1.19 (0.83-1.69)	0.348
e'-wave, cm/s	0.84 (0.78-0.91)	<0.001
E/e' ratio	1.03 (1.02-1.04)	<0.001
TR peak velocity, m/s	1.74 (1.36-2.23)	<0.001

CABG, coronary artery bypass grafting; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LA, left atrium; LV, left ventricle; MR, mitral regurgitation; MV, mitral valve; TR, tricuspid regurgitation.

Supplemental Table 3. The original MIDA risk score and modified version of MIDA risk score used for the current study.

Original MIDA score		MIDA score without PASP	
Variables	Points	Variables	Points
Age ≥ 65 years	3	Age ≥ 65 years	3
Symptoms	3	Symptoms	3
Atrial fibrillation	1	Atrial fibrillation	1
LA dimension ≥ 55 mm	1	LA dimension ≥ 55 mm	1
PASP > 50 mmHg	2	-	-
LV end-systolic diameter ≥ 40 mm	1	LV end-systolic diameter ≥ 40 mm	1
LV ejection fraction $\leq 60\%$	1	LV ejection fraction $\leq 60\%$	1
score range 0–12 points		score range 0–10 points	

LA, left atrium; LV, left ventricle; MIDA, Mitral Regurgitation International Database; mitral regurgitation; PASP, pulmonary artery systolic pressure; TR, tricuspid regurgitation.

Supplemental Table 4. Comparison of the baseline clinical characteristics between the derivation and the validation cohort.

Characteristics	Derivation cohort (n=1,629)	Validation cohort (n=692)	P
Age, year	56 (45–65)	61 (50–69)	<0.001
Male, n (%)	958 (58.8)	382 (55.2)	0.118
Body mass index, kg/m ²	24.2 (21.9–26.5)	23.4 (21.3–25.6)	<0.001
Comorbidities, n (%)			
Hypertension	601 (36.9)	297 (42.9)	0.007
Diabetes	133 (8.2)	89 (12.9)	0.001
Atrial fibrillation	637 (39.1)	303 (43.8)	0.040
Stroke	32 (2.0)	38 (5.5)	<0.001
Myocardial infarction	30 (1.8)	15 (2.2)	0.721
Year of MV surgery			<0.001
2006–2012	783 (48.1)	397 (57.4)	
2012–2020	846 (51.9)	295 (42.6)	
Symptomatic MR, n (%)	548 (33.6)	409 (59.1)	<0.001
Symptoms, n (%)			
Dyspnea	468 (28.7)	355 (51.3)	<0.001
Chest pain	61 (3.7)	48 (6.9)	0.001
Edema	36 (2.2)	43 (6.2)	<0.001
Palpitation	79 (4.8)	89 (12.9)	<0.001
Syncope	16 (1.0)	7 (1.0)	>0.99
Laboratory results			

Hemoglobin, g/dL	13.5 (12.2–14.5)	13.4 (12.0–14.6)	0.259
eGFR, mL/min/1.73m ²	88.3 (73.7–100.3)	79.6 (62.3–93.8)	<0.001
MR etiology, n (%)	0.066		
Degenerative	1,375 (84.4)	604 (87.3)	
Rheumatic	236 (14.5)	77 (11.1)	
Congenital	18 (1.1)	11 (1.6)	
MR surgery type, n (%)	<0.001		
MV repair	1,349 (82.8)	523 (75.6)	
MV replacement (mechanical)	192 (11.8)	75 (10.8)	
MV replacement (bioprosthetic)	88 (5.4)	94 (13.6)	
Concomitant CABG, n (%)	94 (5.8)	30 (4.3)	0.192
Concomitant surgical atrial ablation, n (%)	555 (34.1)	184 (37.3)	0.203
Echocardiography			
LV end-systolic diameter, mm	38 (34–42)	38 (34–42)	0.155
LV end-diastolic diameter, mm	60 (56–64)	60 (55–65)	0.967
LV end-systolic volume, mL	56 (43–71)	55 (42–73)	0.626
LV end-diastolic volume, mL	153 (123–190)	142 (111–177)	<0.001
LV end-systolic volume index, mL/m ²	32.1 (25.4–40.5)	32.8 (24.9–42.7)	0.624
LV end-diastolic volume index, mL/m ²	89.5 (73.3–108.4)	83.1 (67.0–105.2)	0.002
LV ejection fraction, %	63.9 (59.6–67.7)	60.7 (56.0–65.0)	<0.001
LV mass index, g/m ²	132.2 (112.7–153.9)	138.2 (119.5–164.0)	<0.001
LA dimension, mm	51.0 (45.0–57.0)	56.0 (48.6–63.0)	<0.001
E-wave, m/s	1.29 (1.05–1.53)	1.30 (1.07–1.53)	0.813
e'-wave, cm/s	7.4 (6.0–9.1)	7.6 (6.0–9.3)	0.889

E/e' ratio	15.0 (12.0–21.0)	17.1 (12.6–22.0)	0.002
TR peak velocity, m/s	2.8 (2.5–3.3)	2.9 (2.5–3.4)	0.011

Values are expressed in median (interquartile range) or numbers (percentage).

CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrium; LV, left ventricle; MR, mitral regurgitation; MV, mitral valve; TR, tricuspid regurgitation.

Supplemental Table 5. Results of the sensitivity analysis using the combined dataset of derivation and validation cohort for LCA.

Characteristics	Younger population			Older population		P
	Group 1 (n=555)	Group 2 (n=377)	Group 3 (n=282)	Group 4 (n=644)	Group 5 (n=463)	
	<i>Least comorbidities</i>	<i>Men with LV enlargement</i>	<i>Predominantly women and rheumatic MR</i>	<i>Low-risk older patients</i>	<i>High-risk older patients</i>	
Age, year	44 (36–50)	52 (45–58)	51 (42–57)	63 (58–68)	71 (66–75)	<0.001
Men, n (%)	400 (72.1)	377 (100.0)	57 (20.2)	311 (48.3)	195 (42.1)	<0.001
Body mass index, kg/m ²	23.8 (21.5–26.1)	25.1 (22.9–27.3)	22.7 (20.5–24.7)	24.9 (22.8–27.1)	22.7 (20.8–24.8)	<0.001
Comorbidities, n (%)						
Hypertension	95 (17.1)	137 (36.3)	13 (4.6)	396 (61.5)	257 (55.5)	<0.001
Diabetes	5 (0.9)	23 (6.1)	3 (1.1)	86 (13.4)	105 (22.7)	<0.001
Atrial fibrillation	47 (8.5)	231 (61.3)	200 (70.9)	135 (21.0)	327 (70.6)	<0.001
Stroke	2 (0.4)	15 (4.0)	8 (2.8)	14 (2.2)	31 (6.7)	<0.001
Myocardial infarction	4 (0.7)	10 (2.7)	2 (0.7)	9 (1.4)	20 (4.3)	<0.001
Year of MV surgery						<0.001

2006–2013	269 (48.5)	196 (52.0)	181 (64.2)	297 (46.1)	237 (51.2)	
2014–2020	286 (51.5)	181 (48.0)	101 (35.8)	347 (53.9)	226 (48.8)	
Symptomatic MR, n (%)	109 (19.6)	185 (49.1)	155 (55.0)	235 (36.5)	273 (59.0)	<0.001
Symptoms, n (%)						
Dyspnea	85 (15.3)	154 (40.8)	132 (46.8)	203 (31.5)	249 (53.8)	<0.001
Chest pain	22 (4.0)	19 (5.0)	14 (5.0)	27 (4.2)	27 (5.8)	0.643
Edema	6 (1.1)	12 (3.2)	17 (6.0)	10 (1.6)	34 (7.3)	<0.001
Palpitation	20 (3.6)	38 (10.1)	39 (13.8)	33 (5.1)	38 (8.2)	<0.001
Syncope	5 (0.9)	0 (0.0)	4 (1.4)	7 (1.1)	7 (1.5)	0.224
Laboratory results						
Hemoglobin, g/dL	14.0 (13.0–14.9)	14.6 (13.9–15.6)	12.8 (11.7–13.9)	13.0 (12.0–14.1)	12.1 (10.9–13.4)	<0.001
eGFR, mL/min/1.73m ²	102.5 (93.4–111.0)	85.5 (76.1–97.2)	90.2 (75.9–102.1)	83.3 (69.6–92.1)	60.1 (48.4–76.8)	<0.001
MR etiology, n (%)						<0.001
Degenerative	516 (93.0)	351 (93.1)	121 (42.9)	624 (96.9)	367 (79.3)	
Rheumatic	25 (4.5)	22 (5.8)	154 (54.6)	19 (3.0)	93 (20.1)	

Congenital	14 (2.5)	4 (1.1)	7 (2.5)	1 (0.2)	3 (0.6)	
MR surgery type, n (%)						<0.001
MV repair	537 (96.8)	351 (93.1)	109 (38.7)	618 (96.0)	257 (55.5)	
MV replacement (mechanical)	14 (2.5)	26 (6.9)	163 (57.8)	14 (2.2)	50 (10.8)	
MV replacement (bioprosthetic)	4 (0.7)	0 (0.0)	10 (3.5)	12 (1.9)	156 (33.7)	
Concomitant CABG, n (%)	0 (0.0)	16 (4.2)	2 (0.7)	39 (6.1)	67 (14.5)	<0.001
Concomitant surgical atrial ablation, n (%)	43 (8.1)	196 (57.1)	148 (58.0)	122 (20.7)	230 (57.2)	<0.001
Echocardiography						
LV end-systolic diameter, mm	37 (34–40)	43 (40–47)	41 (37.5–45)	34 (31–37)	39 (34–43)	<0.001
LV end-diastolic diameter, mm	60 (56–63)	65 (61–69)	62 (56–66)	57 (54–60)	60 (55–65)	<0.001
LV end-systolic volume, mL	57 (47–68)	78 (60–93)	61 (47–77)	47 (36.5–58)	53 (40–69)	<0.001
LV end-diastolic volume, mL	163.5 (135–194)	190.5 (160–228)	145 (116.5–180)	140 (112–168)	132 (107–167)	<0.001
LV end-systolic volume index, mL/m ²	31.7 (26.7–37.9)	41.6 (32.5–50.3)	37.3 (29.1–48.6)	26.7 (21.8–33.5)	32.7 (25.2–43.3)	<0.001
LV end-diastolic volume index, mL/m ²	90.8 (76.1–109.4)	102.1 (84.6–122.4)	89.5 (72.2–112.4)	82.2 (67.2–97.5)	83.2 (66.9–105.0)	<0.001
LV ejection fraction, %	64.6 (61.0–67.9)	60.0 (54.3–64.4)	58.5 (52.7–62.6)	65.8 (62.2–69.3)	60.0 (55.0–65.3)	<0.001

LV mass index, g/m ²	123.9 (107.2–141.6)	151.6 (131.9–176.1)	135.2 (113.1–162.3)	127.6 (109.1–146.3)	144.7 (122.6–168.1)	<0.001
LA dimension, mm	46.0 (42.0–50.0)	59.0 (56.0–65.0)	59.0 (54.0–64.0)	48.0 (45.0–52.0)	58.0 (51.6–66.0)	<0.001
E-wave, m/s	1.13 (0.96–1.36)	1.43 (1.20–1.66)	1.50 (1.25–1.84)	1.22 (1.01–1.44)	1.36 (1.13–1.60)	<0.001
e'-wave, cm/s	9.0 (7.6–10.9)	8.0 (6.4–9.4)	7.4 (5.9–9.3)	6.8 (5.7–8.0)	6.4 (5.0–8.0)	<0.001
E/e' ratio	12.0 (9.5–15.0)	16.2 (13.0–21.9)	19.0 (14.0–28.0)	17.0 (13.0–21.0)	20.0 (15.0–26.0)	<0.001
TR peak velocity, m/s	2.5 (2.3–2.7)	3.1 (2.7–3.5)	2.9 (2.6–3.3)	2.8 (2.5–3.3)	3.2 (2.9–3.6)	<0.001

Values are expressed in median (interquartile range) or numbers (percentage).

AF, atrial fibrillation; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrium; LCA, latent class analysis; LV, left ventricle; MR, mitral regurgitation; MV, mitral valve; TR, tricuspid regurgitation.

Supplemental Table 6. Results of the LCA analysis using the subgroup of degenerative MR patients in the derivation cohort (n=1,375).

Characteristics	Younger population		Older population		P ^a
	Group 1 (n=502)	Group 2 (n=270)	Group 3 (n=401)	Group 4 (n=202)	
	<i>Least comorbidities</i>	<i>Men with LV enlargement</i>	<i>Low-risk older patients</i>	<i>High-risk older patients</i>	
Age, year	45.0 (37.0–51.0)	53.0 (47.0–60.0)	63.0 (58.0–68.0)	71.0 (67.0–75.0)	<0.001
Men, n (%)	372 (74.1)	248 (91.9)	203 (50.6)	74 (36.6)	<0.001
Body mass index, kg/m ²	24.2 (22.0–26.3)	24.9 (22.7–27.4)	25.3 (23.2–27.5)	23.1 (21.0–24.9)	<0.001
Comorbidities, n (%)					
Hypertension	97 (19.3)	88 (32.6)	267 (66.6)	91 (45.0)	<0.001
Diabetes	5 (1.0)	13 (4.8)	59 (14.7)	32 (15.8)	<0.001
Atrial fibrillation	54 (10.8)	187 (69.3)	104 (25.9)	118 (58.4)	<0.001
Stroke	3 (0.6)	12 (4.4)	6 (1.5)	6 (3.0)	0.002
Myocardial infarction	5 (1.0)	7 (2.6)	5 (1.2)	8 (4.0)	0.033
Year of MV surgery					0.032

2006–2013	241 (48.0)	131 (48.5)	157 (39.2)	93 (46.0)	
2014–2020	261 (52.0)	139 (51.5)	244 (60.8)	109 (54.0)	
Symptomatic MR, n (%)	100 (19.9)	123 (45.6)	113 (28.2)	110 (54.5)	<0.001
Symptoms, n (%)					
Dyspnea	80 (15.9)	99 (36.7)	97 (24.2)	104 (51.5)	<0.001
Chest pain	19 (3.8)	17 (6.3)	12 (3.0)	7 (3.5)	0.173
Edema	3 (0.6)	10 (3.7)	4 (1.0)	10 (5.0)	<0.001
Palpitation	14 (2.8)	22 (8.1)	14 (3.5)	13 (6.4)	0.003
Syncope	5 (1.0)	0 (0.0)	4 (1.0)	4 (2.0)	0.178
Laboratory results					
Hemoglobin, g/dL	14.0 (13.1–14.8)	14.4 (13.5–15.2)	13.1 (12.1–14.1)	12.0 (10.8–13.3)	<0.001
eGFR, mL/min/1.73m ²	101.2 (92.2–109.6)	85.5 (76.6–97.1)	83.9 (71.1–91.6)	61.8 (48.7–82.7)	<0.001
Valve morphology, n (%) ^b					<0.001
Isolated anterior leaflet prolapse	104 (20.7)	40 (14.8)	50 (12.5)	39 (19.6)	
Isolated posterior leaflet prolapse	274 (54.6)	150 (55.6)	270 (67.7)	106 (53.3)	

Bileaflet prolapse	124 (24.7)	80 (29.6)	79 (19.8)	54 (27.1)	
MR surgery type, n (%)					<0.001
MV repair	493 (98.2)	236 (87.4)	395 (98.5)	143 (70.8)	
MV replacement (mechanical)	5 (1.0)	34 (12.6)	3 (0.7)	11 (5.4)	
MV replacement (bioprosthetic)	4 (0.8)	0 (0.0)	3 (0.7)	48 (23.8)	
Concomitant CABG, n (%)	0 (0.0)	14 (5.2)	26 (6.5)	39 (19.3)	<0.001
Concomitant surgical atrial ablation, n (%)	48 (9.6)	171 (63.3)	94 (23.4)	105 (52.0)	<0.001
Echocardiography					
LV end-systolic diameter, mm	37 (34–40)	43 (40–47)	34 (31–37)	38 (33–42)	<0.001
LV end-diastolic diameter, mm	60 (56–63)	65 (61–69)	57 (54–60)	59 (55–64)	<0.001
LV end-systolic volume, mL	58 (47–69)	78 (60–93)	46 (37–57)	52 (40–67)	<0.001
LV end-diastolic volume, mL	166 (138–198)	191 (161–222)	142 (114–166)	137 (114–173)	<0.001
LV end-systolic volume index, mL/m ²	31.7 (26.5–37.8)	41.6 (32.6–50.6)	26.4 (21.9–32.7)	32.5 (25.1–41.9)	<0.001
LV end-diastolic volume index, mL/m ²	92.1 (76.6–109.7)	102.4 (86.2–122.6)	80.9 (67.2–97.3)	87.1 (71.8–107.4)	<0.001
LV ejection fraction, %	65.2 (61.8–68.3)	60.0 (54.2–64.7)	66.4 (62.7–70.2)	62.7 (58.0–67.2)	<0.001

LV mass index, g/m ²	124.8 (108.2–142.1)	151.3 (133.2–175.4)	127.2 (109.1–146.0)	144.6 (122.0–167.4)	<0.001
LA dimension, mm	46.0 (42.0–50.0)	59.0 (55.0–64.0)	48.0 (44.0–52.0)	54.0 (49.0–60.0)	<0.001
E-wave, m/s	1.15 (0.99–1.38)	1.42 (1.21–1.65)	1.20 (0.99–1.43)	1.34 (1.12–1.55)	<0.001
e'-wave, cm/s	9.0 (7.4–10.8)	8.0 (6.4–9.3)	6.7 (5.7–7.9)	6.3 (5.0–8.0)	<0.001
E/e' ratio	12.0 (10.0–15.0)	16.0 (13.0–22.0)	17.0 (13.0–21.0)	18.0 (15.0–23.5)	<0.001
TR peak velocity, m/s	2.5 (2.3–2.8)	3.1 (2.7–3.5)	2.8 (2.5–3.2)	3.2 (2.9–3.6)	<0.001

Values are expressed in median (interquartile range) or numbers (percentage). ^aComparison between 5 groups. ^bData unavailable in 5

degenerative MR patients.

AF, atrial fibrillation; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrium; LCA, latent class analysis; LV, left ventricle; MR, mitral regurgitation; MV, mitral valve; TR, tricuspid regurgitation.

Supplemental Table 7. Partial probabilities of phenogroup membership derived from the latent class analysis model.

Variables	Group				
	1	2	3	4	5
Age, years					
<50	0.707752	0.416556	0.510286	0.017478	1.59×10^{-38}
50–60	0.263756	0.338933	0.362181	0.268637	0.126376
60–70	0.028492	0.189645	0.127533	0.471750	0.408240
≥70	6.18×10^{-95}	0.054866	2.14×10^{-137}	0.242135	0.465384
Sex					
Men	0.703620	1	0.260438	0.497843	0.366273
Women	0.296380	3.90×10^{-34}	0.739562	0.502157	0.633727
Body mass index, kg/m²					
<25	0.608755	0.447318	0.781549	0.504718	0.745615
≥25	0.391245	0.552682	0.218451	0.495282	0.254386
Hypertension					
No	0.796451	0.618034	0.970528	0.376692	0.510819
Yes	0.203549	0.381966	0.029472	0.623308	0.489181
Diabetes					
No	0.987345	0.931831	0.990415	0.864821	0.808357
Yes	0.012656	0.068169	0.009585	0.135179	0.191643
Atrial fibrillation					
No	0.899785	0.366094	0.297973	0.709897	0.311540

Yes	0.100215	0.633906	0.702027	0.290103	0.688460
Symptoms					
No	0.802022	0.554335	0.535881	0.686797	0.545021
Yes	0.197978	0.445665	0.464119	0.313203	0.454979
Anemia^a					
No	0.852485	0.947762	0.717048	0.693525	0.424535
Yes	0.147515	0.052238	0.282952	0.306475	0.575465
eGFR, mL/min/1.73m²					
≥90	0.786799	0.412117	0.601762	0.299329	0.084707
90–60	0.207385	0.545157	0.331747	0.590368	0.484164
60–30	0.004756	0.030953	0.040305	0.110303	0.380378
<30	0.001060	0.011773	0.026186	2.96×10 ⁻¹⁵⁰	0.050751
MV surgery type					
MV repair	0.979446	0.935377	0.392541	0.959586	0.512908
MV replace (mechanical)	0.020554	0.064623	0.558081	0.018262	0.212359
MV replace (bioprosthetic)	2.79×10 ⁻⁵⁹	4.89×10 ⁻⁷²	0.049378	0.022152	0.274732
Concomitant CABG					
No	1	0.939815	0.994153	0.926749	0.817707
Yes	1.18×10 ⁻²⁵¹	0.060185	0.005847	0.073251	0.182293
LV end-systolic diameter, mm					
<40	0.707338	0.225808	0.359048	0.899322	0.525217
≥40	0.292662	0.774192	0.640952	0.100678	0.474783
LV ejection fraction, %					
>60	0.865954	0.513543	0.480412	0.906837	0.472285

≤ 60	0.134046	0.486457	0.519588	0.093163	0.527715
LA dimension, mm					
<55	0.936940	0.261746	0.260389	0.855861	0.416493
≥ 55	0.063060	0.738254	0.739611	0.144139	0.583507
TR peak velocity, m/s					
≤ 2.8	0.793873	0.342921	0.433516	0.533337	0.201027
>2.8	0.206127	0.657079	0.566484	0.466663	0.798973

^amen, hemoglobin <13g/dL; women, hemoglobin <12g/dL.

CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrium; LV, left ventricle; MV, mitral valve; TR, tricuspid regurgitation.

Supplemental Table 8. Baseline characteristics of the study participants according to phenogroups in the validation cohort.

Characteristics	Younger population			Older population		P
	Group 1 (n=81)	Group 2 (n=148)	Group 3 (n=100)	Group 4 (n=151)	Group 5 (n=212)	
	<i>Least comorbidities</i>	<i>Men with LV enlargement</i>	<i>Predominantly women and rheumatic MR</i>	<i>Low-risk older patients</i>	<i>High-risk older patients</i>	
Age, year	43 (37–51)	54.5 (46–61)	49 (38–56.5)	64 (59–70)	71 (66–75)	<0.001
Men, n (%)	56 (69.1)	148 (100.0)	20 (20.0)	67 (44.4)	91 (42.9)	<0.001
Body mass index, kg/m ²	23.2 (21.0–24.8)	24.6 (22.6–26.4)	22.2 (20.2–24.2)	24.2 (22.6–26.5)	22.7 (20.8–24.8)	<0.001
Comorbidities, n (%)						
Hypertension	19 (23.5)	58 (39.2)	4 (4.0)	94 (62.3)	122 (57.5)	<0.001
Diabetes	4 (4.9)	8 (5.4)	1 (1.0)	24 (15.9)	52 (24.5)	<0.001
Atrial fibrillation	1 (1.2)	82 (55.4)	61 (61.0)	16 (10.6)	143 (67.5)	<0.001
Stroke	1 (1.2)	4 (2.7)	4 (4.0)	7 (4.6)	22 (10.4)	0.004
Myocardial infarction	0 (0.0)	3 (2.0)	0 (0.0)	4 (2.6)	8 (3.8)	0.149
Year of MV surgery						0.204

2006–2013	41 (50.6)	83 (56.1)	65 (65.0)	93 (61.6)	115 (54.2)	
2014–2020	40 (49.4)	65 (43.9)	35 (35.0)	58 (38.4)	97 (45.8)	
Symptomatic MR, n (%)	29 (35.8)	87 (58.8)	66 (66.0)	74 (49.0)	153 (72.2)	<0.001
Symptoms, n (%)						
Dyspnea	22 (27.2)	76 (51.4)	59 (59.0)	62 (41.1)	136 (64.2)	<0.001
Chest pain	5 (6.2)	5 (3.4)	5 (5.0)	11 (7.3)	22 (10.4)	0.113
Edema	2 (2.5)	7 (4.7)	7 (7.0)	5 (3.3)	22 (10.4)	0.025
Palpitation	12 (14.8)	21 (14.2)	20 (20.0)	11 (7.3)	25 (11.8)	0.051
Syncope	1 (1.2)	0 (0.0)	1 (1.0)	2 (1.3)	3 (1.4)	0.727
Laboratory results						
Hemoglobin, g/dL	14.4 (13.1–15.4)	14.7 (13.9–15.6)	13.0 (11.6–13.8)	13.0 (12.1–13.9)	12.2 (10.9–13.4)	<0.001
eGFR, mL/min/1.73m ²	100.5 (89.8–110.0)	82.9 (70.6–96.3)	86.6 (71.5–98.4)	81.9 (67.9–92.2)	59.1 (46.4–75.4)	<0.001
MR etiology, n (%)						<0.001
Degenerative	72 (88.9)	142 (95.9)	58 (58.0)	149 (98.7)	183 (86.3)	
Rheumatic	2 (2.5)	6 (4.1)	39 (39.0)	2 (1.3)	28 (13.2)	

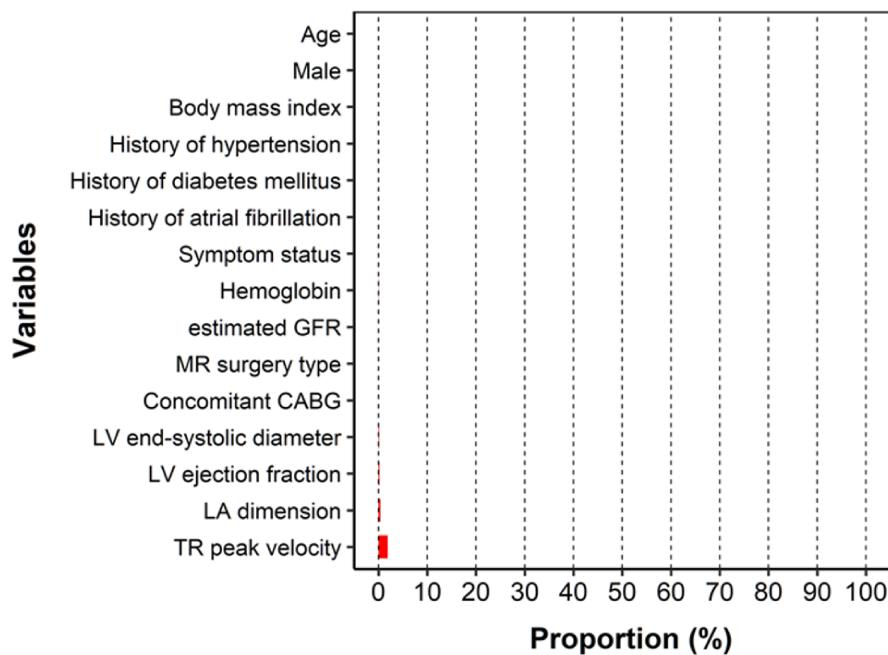
Congenital	7 (8.6)	0 (0.0)	3 (3.0)	0 (0.0)	1 (0.5)	
MR surgery type, n (%)						<0.001
MV repair	80 (98.8)	137 (92.6)	44 (44.0)	142 (94.0)	120 (56.6)	
MV replacement (mechanical)	1 (1.2)	11 (7.4)	49 (49.0)	4 (2.6)	10 (4.7)	
MV replacement (bioprosthetic)	0 (0.0)	0 (0.0)	7 (7.0)	5 (3.3)	82 (38.7)	
Concomitant CABG, n (%)	0 (0.0)	4 (2.7)	0 (0.0)	6 (4.0)	20 (9.4)	<0.001
Concomitant surgical atrial ablation, n (%)	2 (3.6)	53 (49.1)	40 (54.1)	13 (12.6)	76 (50.0)	<0.001
Echocardiography						
LV end-systolic diameter, mm	36.5 (34–40)	41 (40–46)	40 (36–45)	34 (31–37)	38 (34–43)	<0.001
LV end-diastolic diameter, mm	59 (55–62)	64 (60–69)	62.5 (56–66)	56 (52–60)	60 (55–65)	<0.001
LV end-systolic volume, mL	50.2 (45–67)	75 (57–91)	59 (41–80)	47 (31–64)	52 (41–67)	<0.001
LV end-diastolic volume, mL	146 (121–165)	175 (145–207)	131 (97–177)	131 (100–169)	123 (101–150)	<0.001
LV end-systolic volume index, mL/m ²	29.7 (25.3–37.5)	40.7 (31.6–51.0)	35.7 (26.3–48.6)	28.2 (20.2–35.4)	32.0 (24.8–41.1)	<0.001
LV end-diastolic volume index, mL/m ²	81.2 (71.1–91.4)	99.2 (82.3–113.5)	85.5 (64.5–106.0)	80.9 (65.1–95.9)	77.4 (62.4–95.9)	<0.001
LV ejection fraction, %	62.2 (58.0–65.2)	58.8 (54.0–63.0)	58.0 (52.0–61.8)	64.0 (61.0–69.0)	59.0 (54.0–64.0)	<0.001

LV mass index, g/m ²	121.8 (103.6–141.6)	151.9 (125.0–176.4)	141.8 (121.9–179.4)	131.1 (114.5–149.7)	145.5 (125.0–167.5)	<0.001
LA dimension, mm	46.0 (41.0–50.0)	59.0 (56.0–65.0)	60.0 (54.0–65.3)	50.0 (45.3–54.0)	59.0 (53.0–67.0)	<0.001
E-wave, m/s	1.10 (0.90–1.30)	1.36 (1.10–1.58)	1.40 (1.22–1.60)	1.29 (1.04–1.42)	1.30 (1.07–1.60)	<0.001
e'-wave, cm/s	9.6 (8.0–11.0)	8.3 (6.7–9.4)	8.0 (5.8–9.9)	7.0 (5.9–8.2)	6.7 (5.3–8.3)	<0.001
E/e' ratio	11.0 (9.0–14.0)	16.1 (12.2–20.4)	19.0 (14.4–27.6)	18.0 (13.8–20.4)	20.0 (14.1–26.0)	<0.001
TR peak velocity, m/s	2.4 (2.2–2.8)	3.1 (2.5–3.7)	2.8 (2.4–3.2)	2.8 (2.5–3.3)	3.1 (2.8–3.6)	<0.001

Values are expressed in median (interquartile range) or numbers (percentage).

AF, atrial fibrillation; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrium; LV, left ventricle; MR, mitral regurgitation; MV, mitral valve; TR, tricuspid regurgitation.

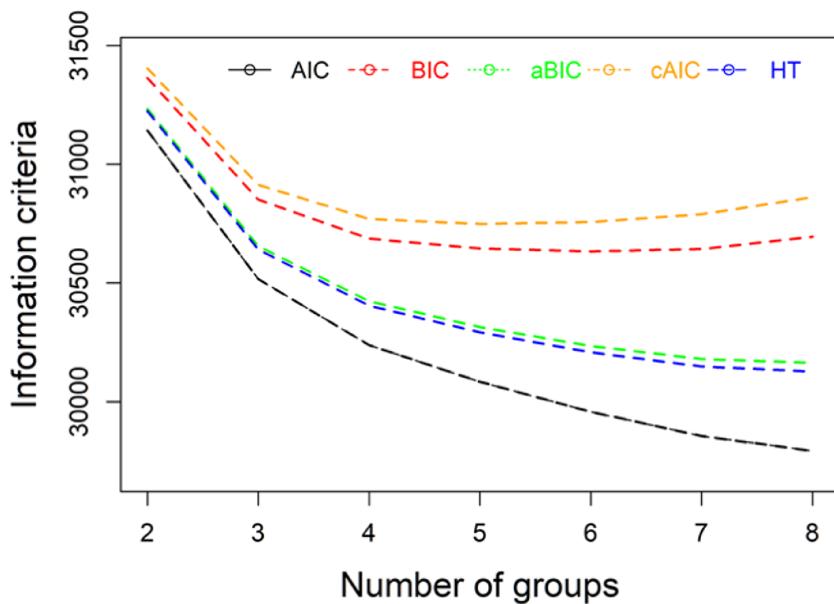
Supplemental Figure 1. Proportion of missing variables used for latent class analysis in the derivation cohort.



CABG, coronary artery bypass grafting; GFR, glomerular filtration rate; LA, left atrium; LV, left ventricle; TR, tricuspid regurgitation.

Supplemental Figure 2. Comparison of information criteria to choose the most optimal number of phenogroups.

Five information criteria (AIC, BIC, aBIC, cAIC, and HT) were used to identify the optimal number of groups ($=k$) in the LCA model. Lower values of these criteria indicate better statistical fitting of the corresponding model. The cAIC was the lowest when $k=5$ (30749.03), and BIC was the lowest when $k=6$ (30632.28). Other information criteria gradually decreased as the number of groups increased from 2 to 8. To prevent overfitting and to ensure clinical interpretability (meaning that a very small proportion of the group would not be clinically significant or meaningful), the minimal proportion of each group was set at 10%. Based on these criteria, the optimal number of groups was 5.

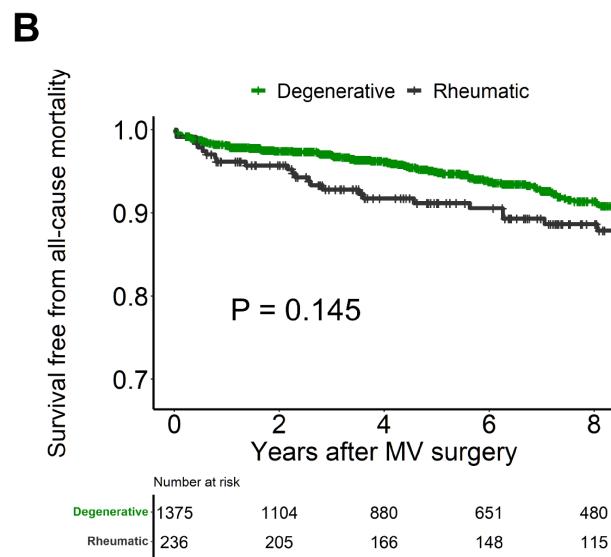
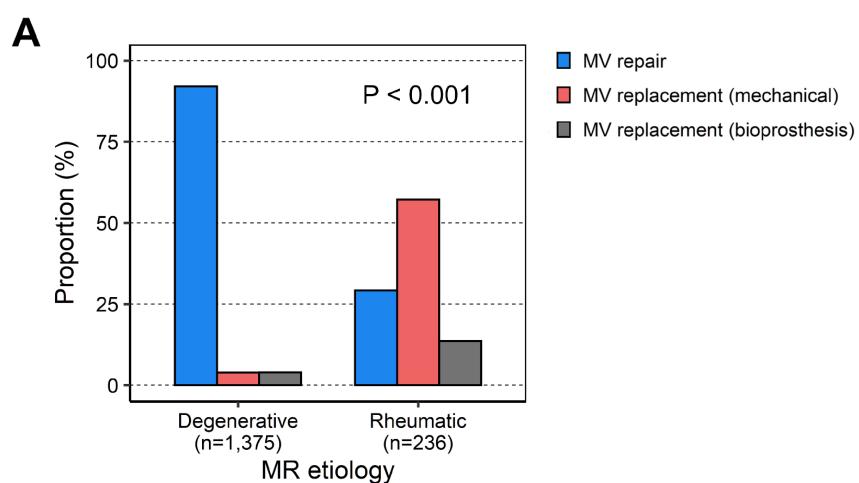


AIC, Akaike Information Criterion; aBIC, adjusted Bayesian Information Criterion; BIC, Bayesian Information Criterion; cAIC, corrected Akaike Information Criterion; HT, Hurvich and Tsai Criterion; LCA, latent class analysis.

Supplemental Figure 3. Types of surgery performed and long-term outcomes according to the degenerative and rheumatic MR etiology in the derivation cohort.

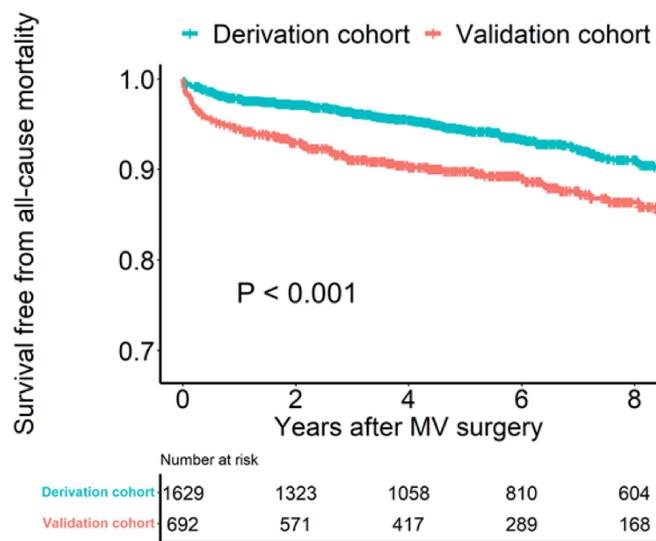
Congenital MR patients were not included in this analysis because of the small number of patients (n=18).

(A) Types of surgery performed by MR etiology. (B) Kaplan-Meier survival curves of all-cause mortality according to the MR etiology.



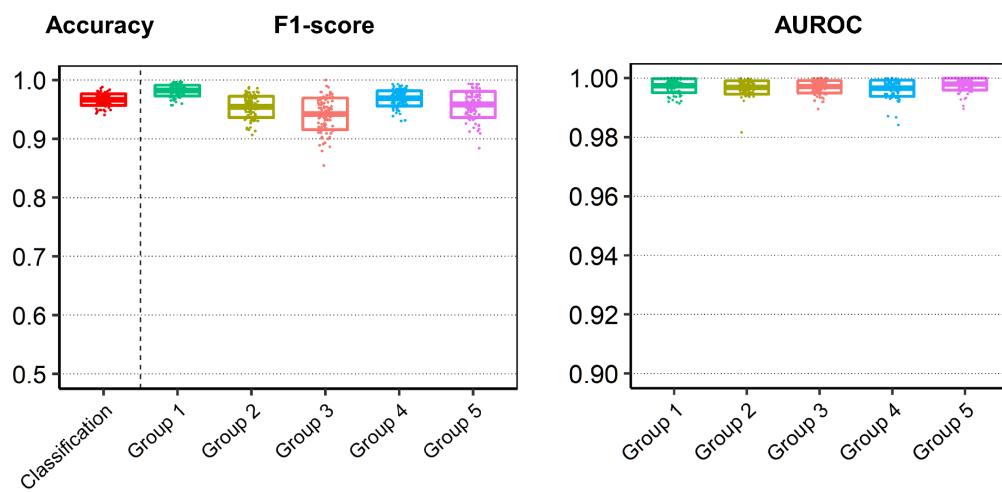
MR, mitral regurgitation; MV, mitral valve.

Supplemental Figure 4. Comparison of survival after MV surgery between the derivation and validation cohort.



MV, mitral valve.

Supplemental Figure 5. Internal validation analysis testing the stability of the group membership.



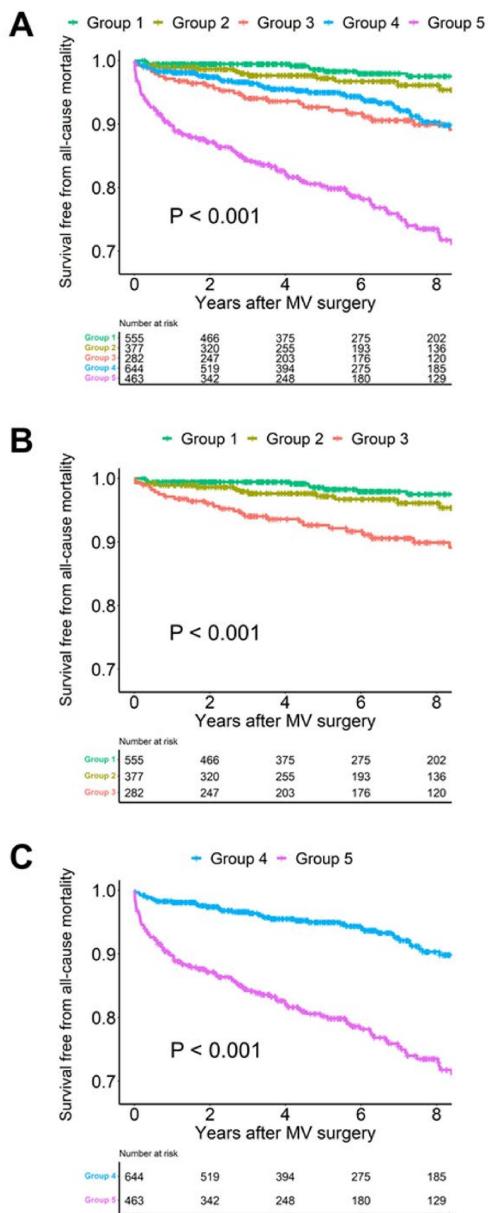
Metrics	Group 1	Group 2	Group 3	Group 4	Group 5
Accuracy	0.966 (0.010)				
F1-score	0.982 (0.009)	0.954 (0.018)	0.942 (0.027)	0.968 (0.013)	0.958 (0.022)
AUROC	0.997 (0.002)	0.997 (0.002)	0.997 (0.002)	0.996 (0.003)	0.998 (0.002)

Values are expressed as mean (standard deviation).

AUROC, area under the receiver operating characteristic curve.

Supplemental Figure 6. Survival after MV surgery according to phenogroups in the sensitivity analysis using the combined dataset of derivation and validation cohort.

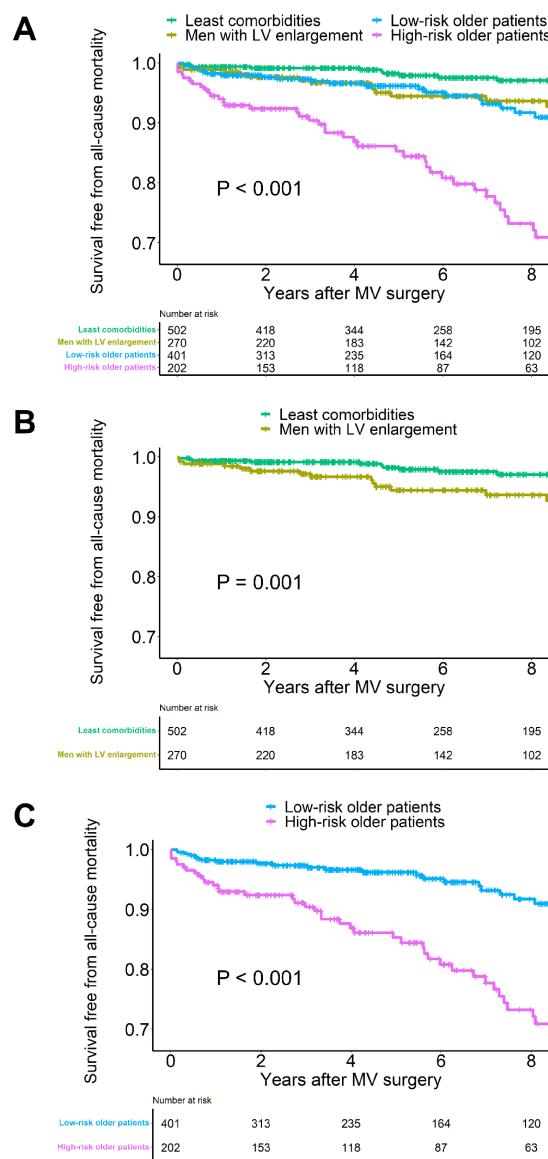
Kaplan-Meier survival curves of (A) entire groups (1–5), (B) younger groups (1–3), and (C) older groups (4–5).



MV, mitral valve.

Supplemental Figure 7. Survival after MV surgery according to phenogroups in the subgroup analysis of patients with degenerative MR.

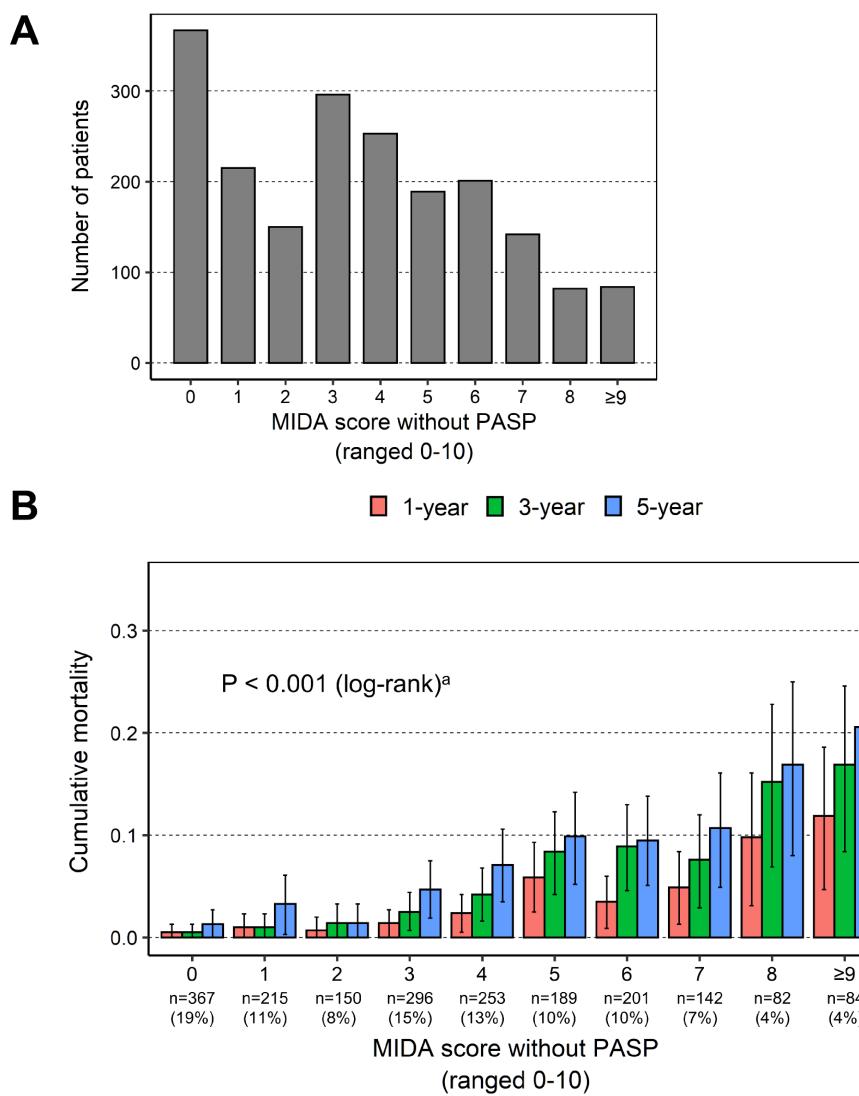
Kaplan-Meier survival curves of (A) entire groups, (B) younger groups, and (C) older groups.

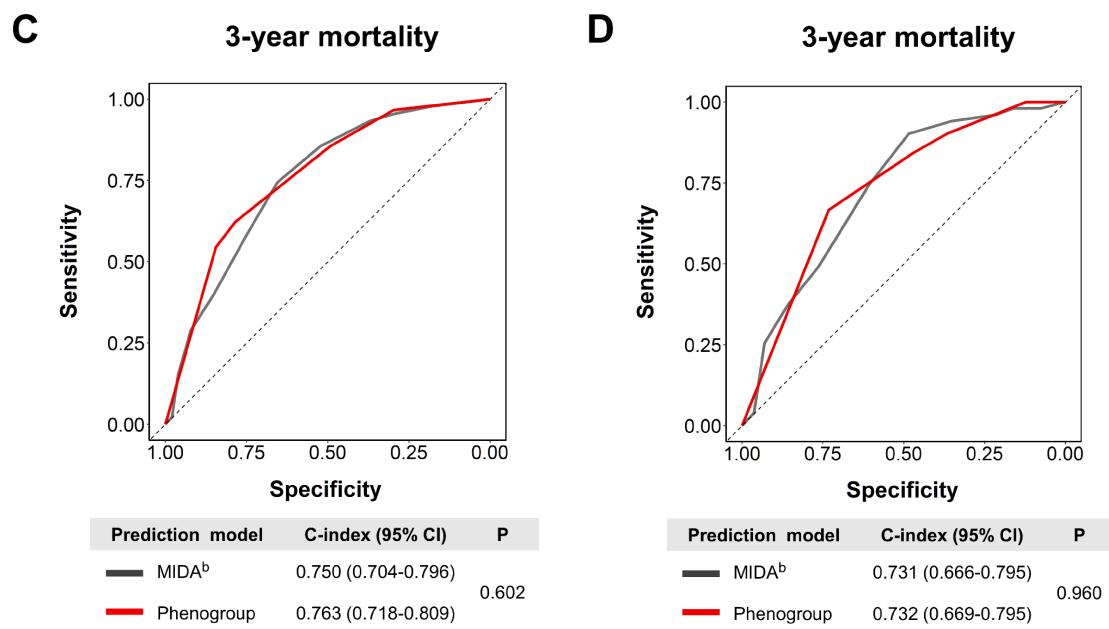


MR, mitral regurgitation; MV, mitral valve.

Supplemental Figure 8. The predictive performance of MIDA score and phenogroup membership for 3-year mortality after MV surgery in degenerative MR patients.

(A) The distribution of MIDA risk score without PASP in patients with degenerative MR across the entire cohort is shown (n=1,979). (B) The MIDA risk score demonstrated effective risk stratification after MV surgery in patients with degenerative MR across the entire cohort (n=1,979). The phenogroup membership showed similar predictive performance as the MIDA score (C) in the entire cohort (n=1,979) and (D) in the validation cohort (n=604).





^aP<0.001 in 1-year, 3-year and 5-year cumulative mortality; ^bMIDA risk score without PASP

CI, confidence interval; MIDA, Mitral Regurgitation International Database; MR, mitral regurgitation; MV, mitral valve.