

Supplemental Online Content

Kwak S, Sun BJ, Lee S, et al. Sex-specific association of left ventricular function with mortality in severe mitral regurgitation. *JAMA Netw Open*. 2025;8(3):e252420. doi:10.1001/jamanetworkopen.2025.2420

eMethods. Echocardiography measurements

eTable 1. Number of mortality events in men and women by different time periods

eTable 2. Number of patients and mortality events according to symptom status, left ventricular ejection fraction, and left ventricular global longitudinal strain groups by sex

eTable 3. Baseline characteristics of propensity-matched cohort by sex

eTable 4. Baseline characteristics of asymptomatic study patients by sex

eFigure 1. Proportion of missing values for the main study variables

eFigure 2. Distribution of left ventricular ejection fraction and left ventricular global longitudinal strain values according to sex

eFigure 3. Mortality according to sex in the entire cohort and the propensity-matched cohort

eFigure 4. Mortality according to left ventricular systolic function and sex stratified by the different time period

eFigure 5. Mortality according to left ventricular systolic function and sex in the propensity-matched cohort

eFigure 6. Mortality according to left ventricular systolic function and sex in asymptomatic individuals

eFigure 7. Relationship between left ventricular systolic function and mortality by sex in asymptomatic individuals without evidence of obstructive coronary artery disease

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods. Echocardiography measurements

LV dimensions were measured from the parasternal view, perpendicular to the LV long axis. LV end-diastolic and end-systolic volumes were measured by tracing the endocardial border in the apical 2-chamber and 4-chamber views. LV ejection fraction was calculated using the biplane Simpson's method. The LV mass was calculated according to the recommended formula and indexed to the body surface area. The anteroposterior dimension of the left atrium (LA) was measured at the end of systole in the standard parasternal views. The early diastolic velocity of the mitral inflow (E-wave velocity) was acquired from the apical 4-chamber view at the tip of the MV. The septal e'-wave was obtained at the medial side of the mitral annulus. Tricuspid regurgitation (TR) peak velocity was measured from the right ventricle-focused apical 4-chamber view. The severity of MR was determined using qualitative, semiquantitative, and quantitative methods following contemporary guidelines.

eTable 1. Number of mortality events in men and women by different time periods

	Men (n=1,088)	Women (n=598)	Log-rank P
30-day mortality	7 (0.6)	3 (0.5)	0.72
1-year mortality	28 (2.6)	20 (3.3)	0.37
5-year mortality	59 (5.4)	43 (7.2)	0.15
8-year mortality	78 (7.2)	66 (11.0)	0.01
Overall mortality	117 (10.8)	103 (17.2)	<0.001

eTable 2. Number of patients and mortality events according to symptom status, left ventricular ejection fraction, and left ventricular global longitudinal strain groups by sex

	Men (n=1,088)		Women (n=598)	
	Asymptomatic (n=718)	Symptomatic (n=370)	Asymptomatic (n=332)	Symptomatic (n=266)
LVEF >60%	n=535 (39 deaths [7.3%])	n=218 (28 deaths [12.8%])	n=264 (24 deaths [9.1%])	n=189 (32 deaths [16.9%])
LVEF 55–60%	n=121 (12 deaths [9.9%])	n=81 (11 deaths [13.6%])	n=42 (7 deaths [16.7%])	n=46 (19 deaths [41.3%])
LVEF ≤55%	n=62 (12 deaths [19.4%])	n=71 (15 deaths [21.1%])	n=25 (6 deaths [24.0%])	n=31 (15 deaths [48.4%])
LV-GLS ≥23.4%	n=269 (19 deaths [7.1%])	n=71 (10 deaths [14.1%])	n=152 (11 deaths [7.2%])	n=81 (16 deaths [19.8%])
LV-GLS 19.9–23.4%	n=229 (15 deaths [6.6%])	n=136 (17 deaths [12.5%])	n=97 (12 deaths [12.4%])	n=90 (16 deaths [17.8%])
LV-GLS <19.9%	n=220 (29 deaths [13.2%])	n=163 (27 deaths [16.6%])	n=83 (14 deaths [16.9%])	n=95 (34 deaths [35.8%])

There was one female patient with missing LVEF data who was omitted from the LVEF categorization.

LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain

eTable 3. Baseline characteristics of propensity-matched cohort by sex

Characteristics	Men (n=578)	Women (n=578)	P
Age, years	60 (51–68)	62 (51–69)	0.207
Body mass index, kg/m ²	24.4 (22.4–26.4)	23.8 (21.4–26.3)	0.005
Comorbidities			
Hypertension	250 (43.3)	244 (42.2)	0.766
Diabetes mellitus	71 (12.3)	53 (9.2)	0.106
Atrial fibrillation	243 (42.0)	185 (32.0)	0.001
Stroke	13 (2.2)	23 (4.0)	0.128
Myocardial infarction	9 (1.6)	10 (1.7)	>0.99
Symptomatic MR	252 (43.6)	247 (42.7)	0.812
Symptoms			
Dyspnea	218 (37.7)	219 (37.9)	>0.99
Chest pain	32 (5.5)	19 (3.3)	0.086
Edema	23 (4.0)	22 (3.8)	>0.99
Palpitation	39 (6.7)	41 (7.1)	0.908
Syncope	4 (0.7)	8 (1.4)	0.384
Laboratory results			
Hemoglobin, g/dL	14.1 (13.0–14.9)	12.5 (11.5–13.2)	<0.001
eGFR, mL/min/1.73m ²	84.5 (71.0–94.8)	86.4 (67.3–98.7)	0.340
MR surgery type			0.145
MV repair	517 (89.4)	507 (87.7)	
MV replacement (mechanical)	26 (4.5)	20 (3.5)	
MV replacement (bioprosthetic)	35 (6.1)	51 (8.8)	
Concomitant CABG	40 (6.9)	29 (5.0)	0.214
Concomitant surgical atrial ablation	213 (36.9)	168 (29.1)	0.006
Echocardiography			
LV end-systolic diameter, mm	38 (34–42)	35 (32–39)	<0.001
LV end-diastolic diameter, mm	61 (57–65)	57 (53–62)	<0.001
LV end-systolic volume, mL	59.0 (48.0–74.0)	46.0 (36.0–59.0)	<0.001
LV end-systolic volume index, mL/m ²	32.8 (26.7–41.0)	28.9 (22.5–37.8)	<0.001
LV end-diastolic volume, mL	167.0 (137.0–196.5)	133.0 (110.0–163.0)	<0.001

LV end-diastolic volume index, mL/m ²	92.2 (75.5–109.6)	85.6 (68.6–103.4)	<0.001
LVEF, %	63.0 (59.3–67.2)	64.6 (60.2–68.6)	<0.001
LV mass index, g/m ²	136.9 (119.5–156.8)	128.2 (108.6–152.1)	<0.001
LA dimension, mm	52 (47–59)	50 (44–56)	<0.001
E-wave, m/s	1.14 (0.82–1.41)	1.16 (0.75–1.43)	0.670
e'-wave, cm/s	7.3 (6.0– 9.0)	7.0 (5.8– 9.0)	0.011
E/e' ratio	15 (12–20)	17 (13–22)	0.002
TR peak velocity, m/s	2.8 (2.5– 3.3)	2.9 (2.6– 3.4)	0.001
LV-GLS, %	20.9 (18.3–23.7)	22.1 (19.1–25.1)	<0.001

Values are expressed as median (interquartile range) or numbers (percentage)

CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain; MR, mitral regurgitation; MV, mitral valve; TR, tricuspid regurgitation

eTable 4. Baseline characteristics of asymptomatic study patients by sex

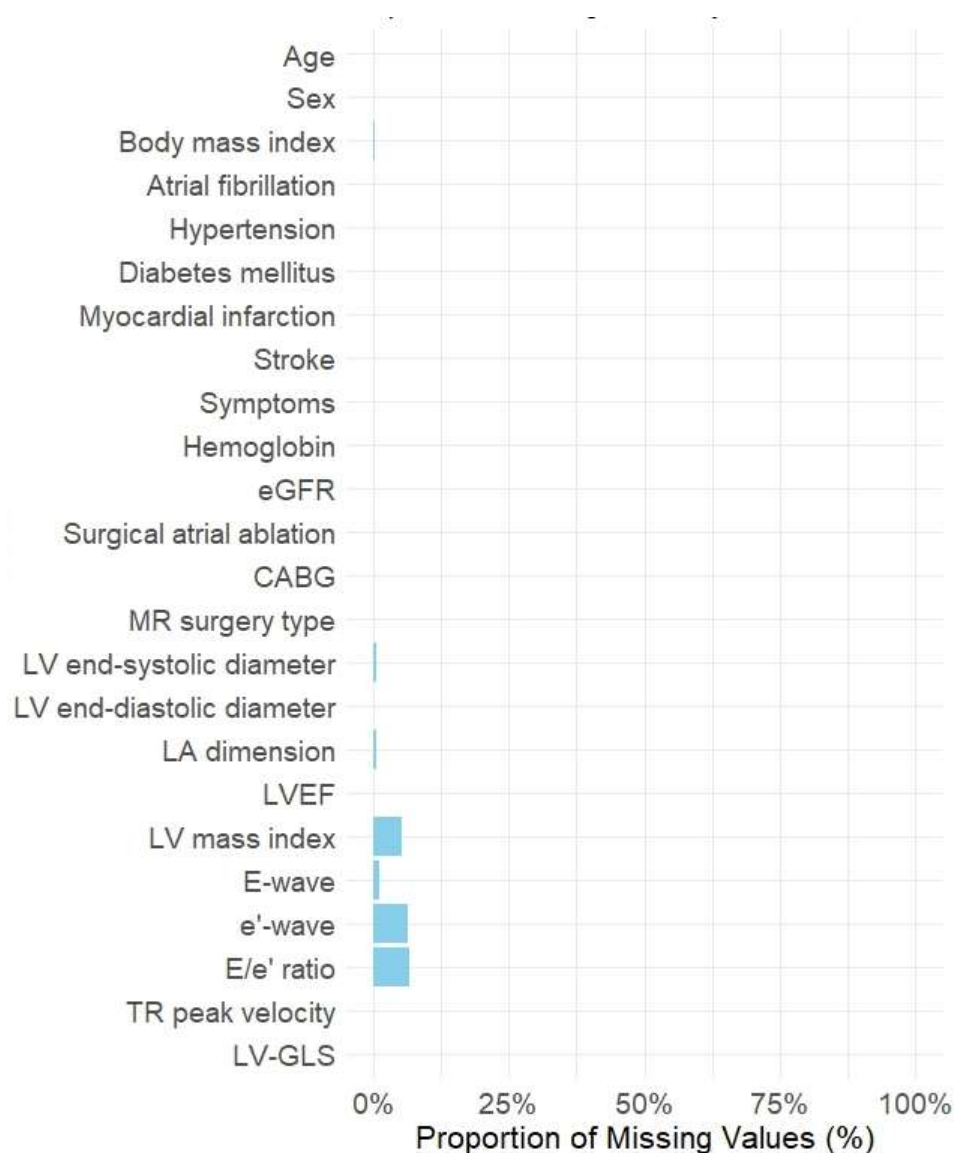
Characteristics	Men (n=718)	Women (n=332)	P
Age, years	54 (45–62)	60 (50–69)	<0.001
Body mass index, kg/m ²	24.8 (22.8–26.9)	23.5 (21.6–26.3)	<0.001
Comorbidities			
Hypertension	292 (40.7)	142 (42.8)	0.565
Diabetes mellitus	61 (8.5)	25 (7.5)	0.682
Atrial fibrillation	220 (30.6)	99 (29.8)	0.844
Stroke	15 (2.1)	15 (4.5)	0.046
Myocardial infarction	17 (2.4)	6 (1.8)	0.726
Laboratory results			
Hemoglobin, g/dL	14.2 (13.4–15.0)	12.4 (11.5–13.2)	<0.001
eGFR, mL/min/1.73m ²	89.7 (77.0–101.0)	89.0 (72.0–100.4)	0.455
MR surgery type			<0.001
MV repair	678 (94.4)	300 (90.4)	
MV replacement (mechanical)	29 (4.0)	8 (2.4)	
MV replacement (bioprosthetic)	11 (1.5)	24 (7.2)	
Concomitant CABG	28 (3.9)	13 (3.9)	>0.99
Concomitant surgical atrial ablation	199 (27.7)	90 (27.1)	0.896
Echocardiography			
LV end-systolic diameter, mm	38 (35–42)	35 (32–39)	<0.001
LV end-diastolic diameter, mm	61 (57–65)	57 (53–62)	<0.001
LV end-systolic volume, mL	60.0 (50.0–73.0)	46.0 (37.0–57.0)	<0.001
LV end-systolic volume index, mL/m ²	32.3 (26.9–39.6)	29.0 (23.1–37.1)	<0.001
LV end-diastolic volume, mL	170.0 (141.5–201.0)	135.0 (110.0–160.0)	<0.001
LV end-diastolic volume index, mL/m ²	91.5 (76.6–109.5)	86.7 (68.6–101.4)	<0.001
LVEF, %	64.0 (60.0–67.4)	64.8 (60.9–69.0)	0.003
LV mass index, g/m ²	133.2 (114.4–152.7)	127.0 (107.3–150.3)	0.002
LA dimension, mm	50.0 (45.0–56.0)	48.0 (44.0–54.0)	0.018
E-wave, m/s	1.11 (0.88–1.38)	1.18 (0.91–1.43)	0.034
e'-wave, cm/s	8.1 (6.7–9.9)	7.2 (5.9–9.0)	<0.001
E/e' ratio	13 (10–18)	16 (13–20)	<0.001

TR peak velocity, m/s	2.6 (2.4–3.0)	2.8 (2.5–3.3)	<0.001
LV-GLS, %	22.0 (19.0–24.8)	22.9 (19.9–25.5)	0.008

Values are expressed as median (interquartile range) or numbers (percentage)

CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain; MV, mitral valve; TR, tricuspid regurgitation

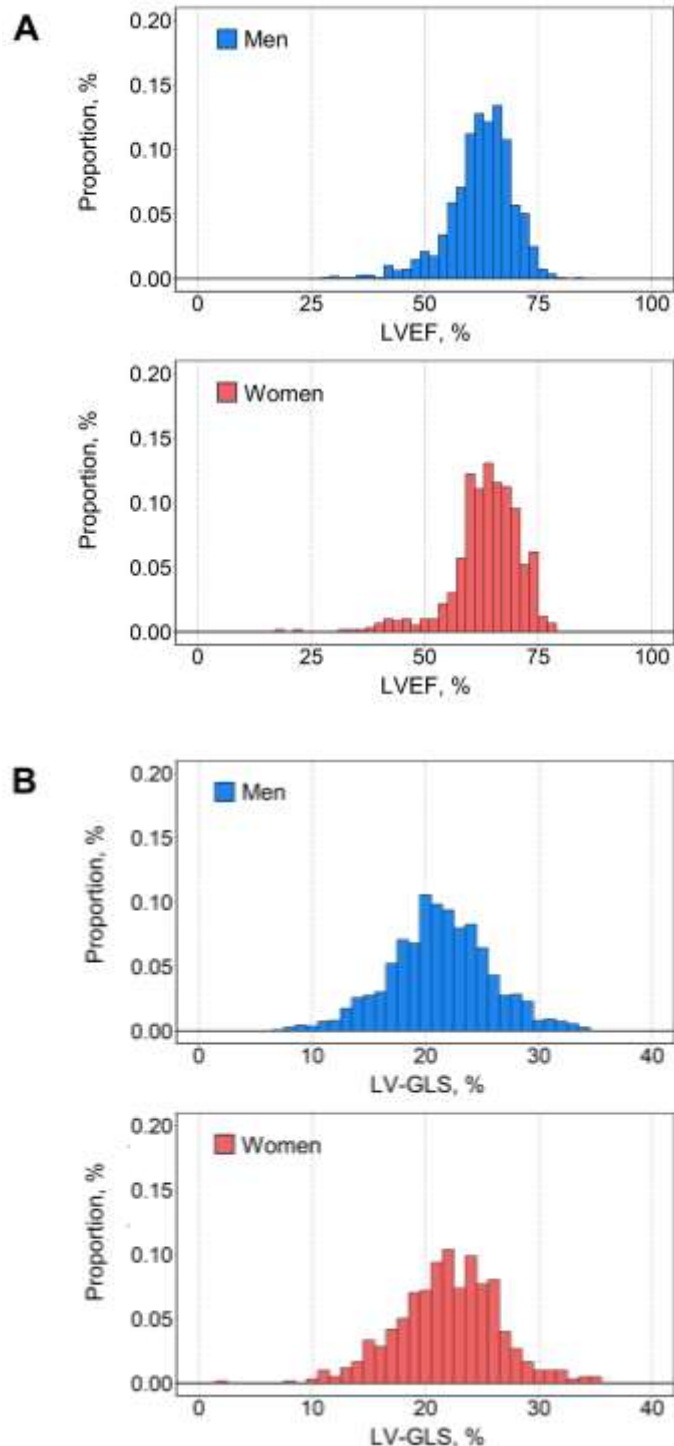
eFigure 1. Proportion of missing values for the main study variables



CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; LA, left atrial; LV, left ventricle; LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain; MR, mitral regurgitation; TR, tricuspid regurgitation.

eFigure 2. Distribution of left ventricular ejection fraction and left ventricular global longitudinal strain values according to sex

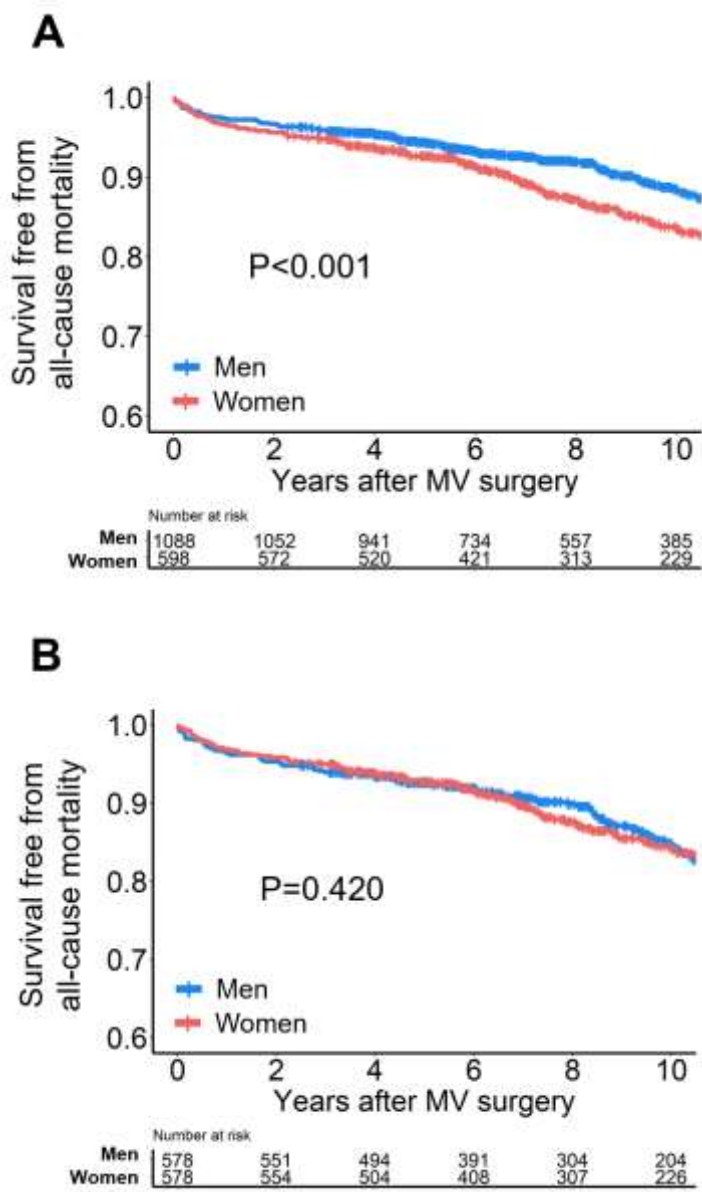
For LVEF, the data are grouped in intervals of 2%, and for LV-GLS, the intervals are 1%.



LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain

eFigure 3. Mortality according to sex in the entire cohort and the propensity-matched cohort

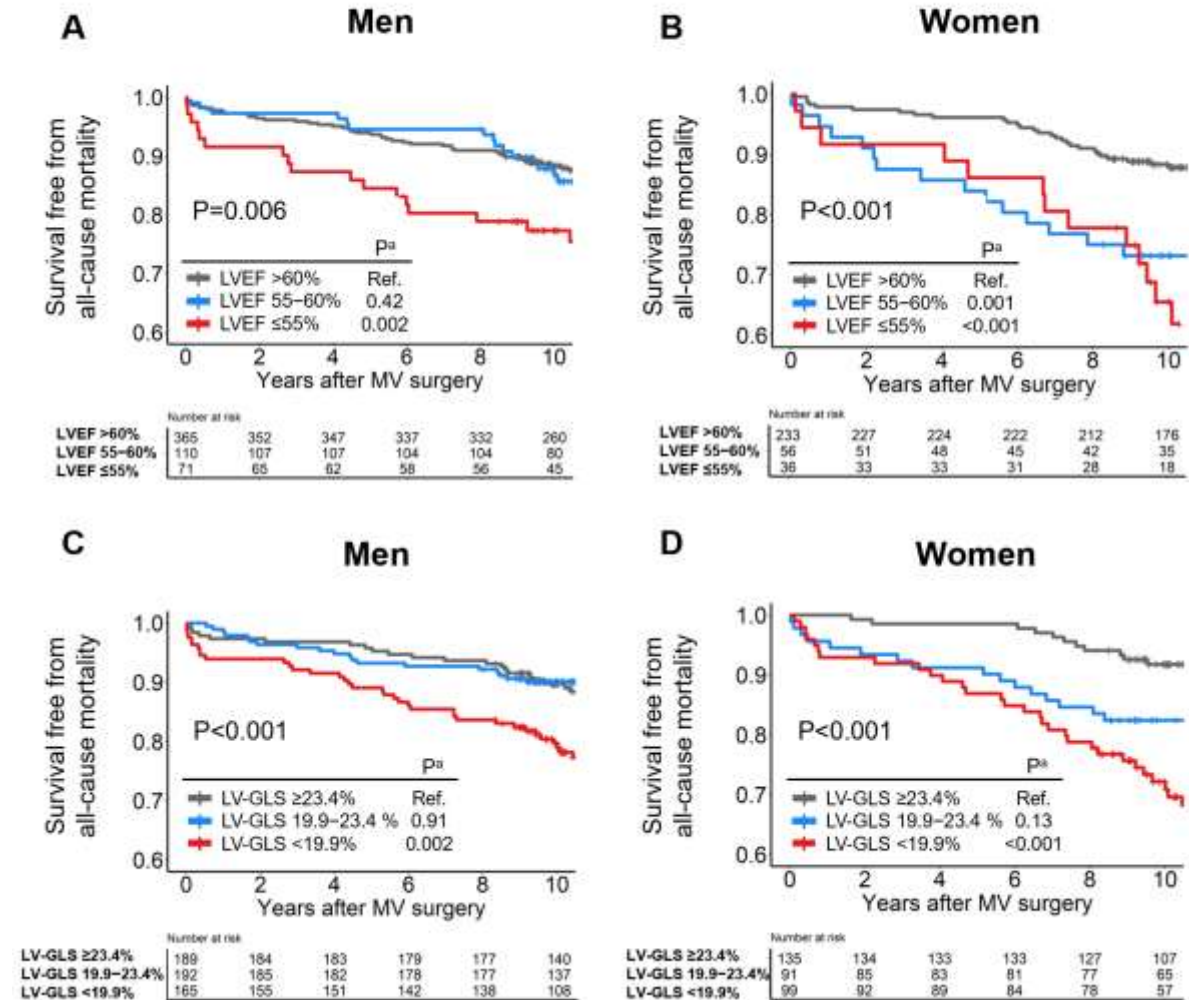
Survival free from all-cause mortality in (A) the entire population and (B) the propensity-matched cohort.



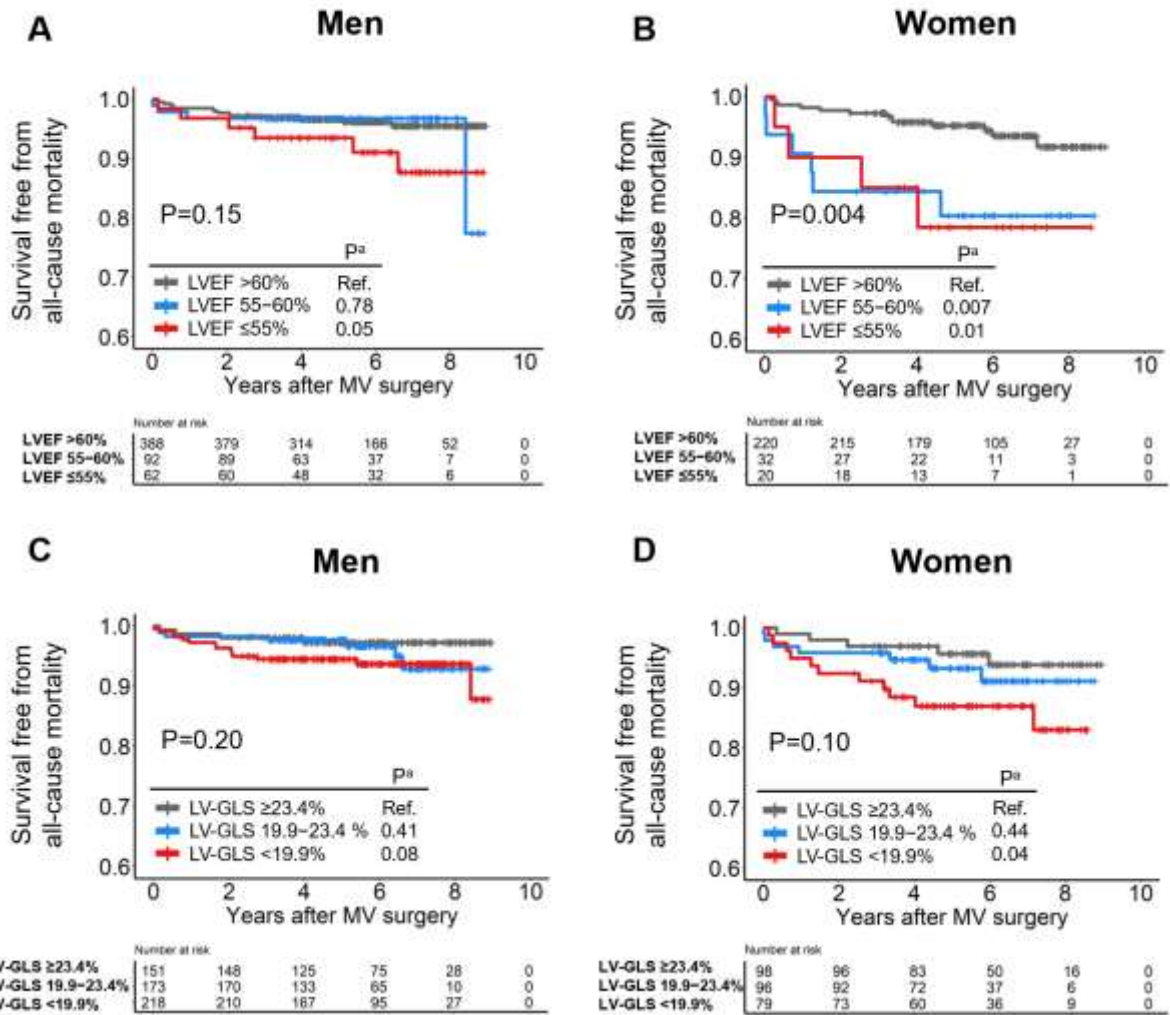
MV, mitral valve

eFigure 4. Mortality according to left ventricular systolic function and sex stratified by the different time period

Period 2006 to 2014



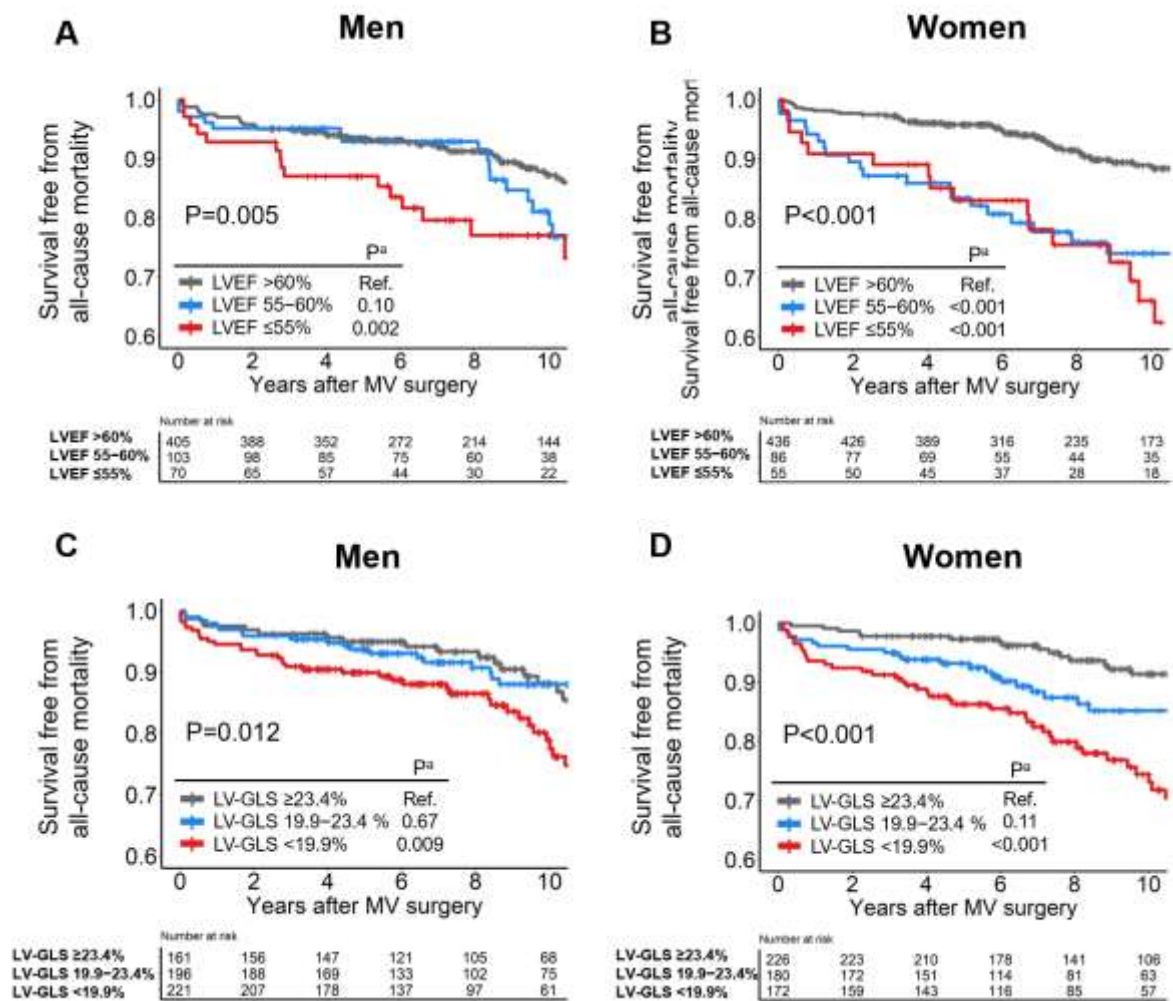
Period 2015 to 2020



^aP value for pairwise comparison with the LVEF >60% or LV-GLS ≥23.4%

LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain

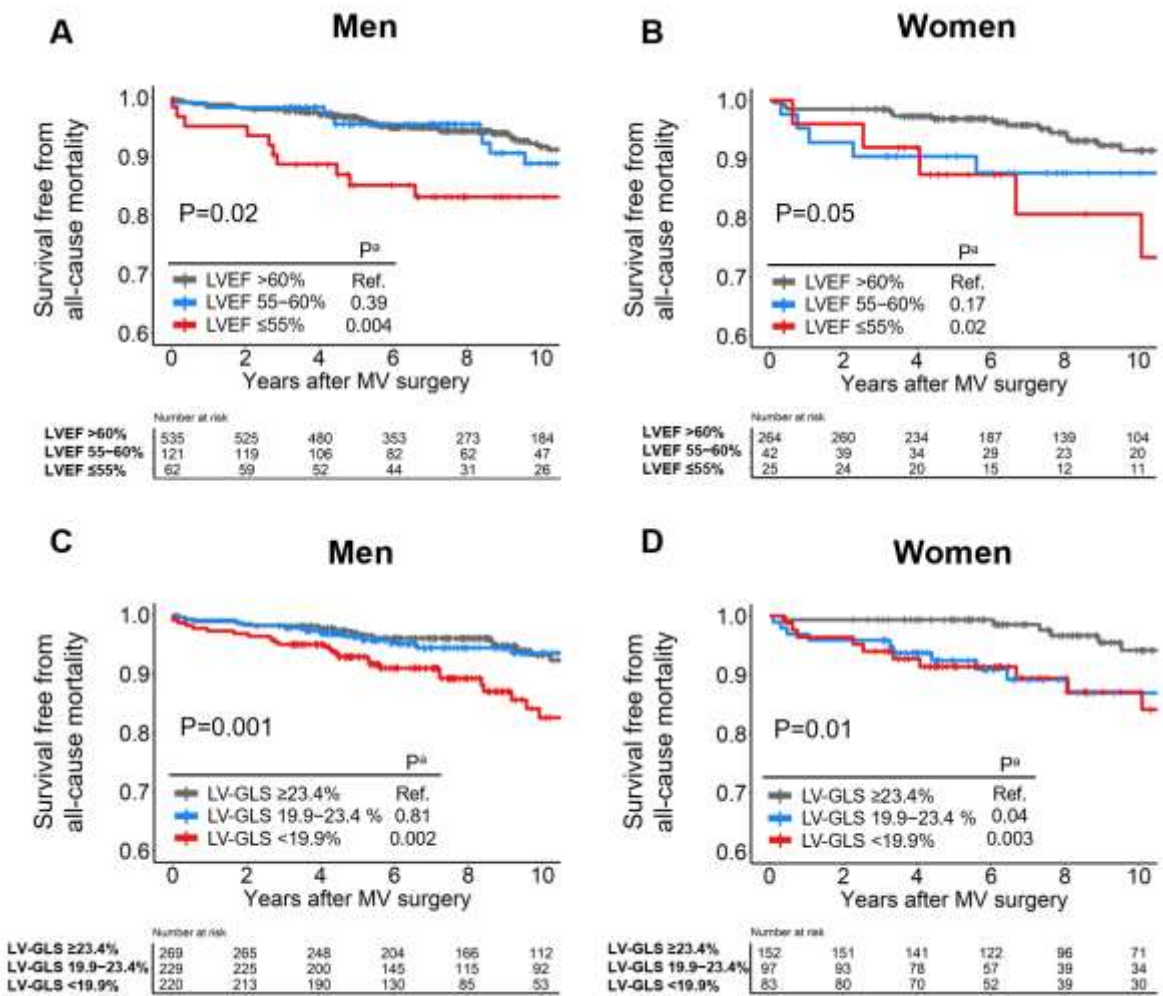
eFigure 5. Mortality according to left ventricular systolic function and sex in the propensity-matched cohort



^aP value for pairwise comparison with the LVEF >60% or LV-GLS ≥23.4%

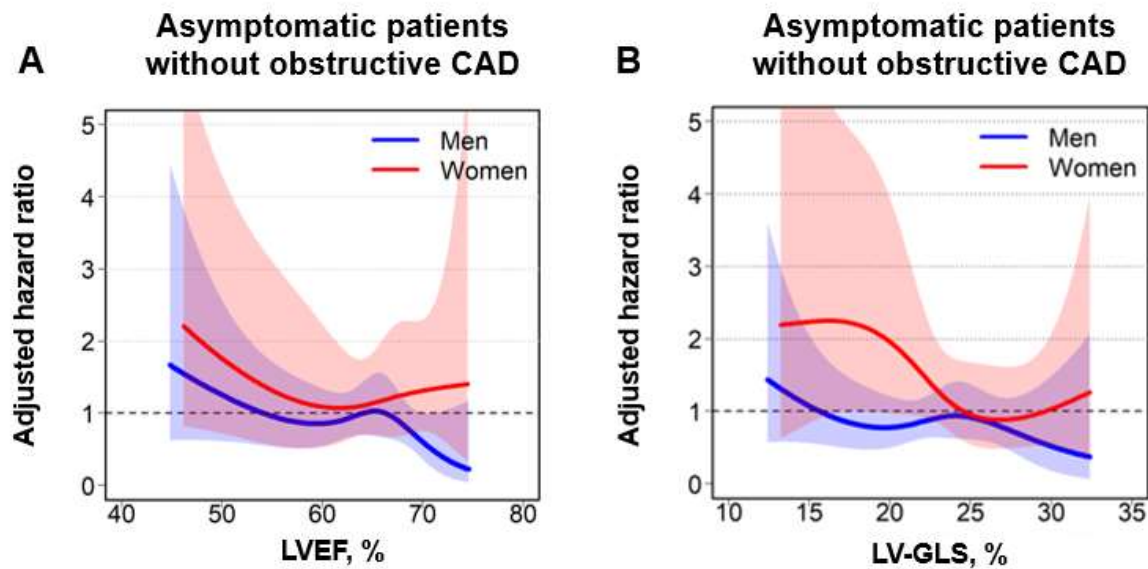
LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain

eFigure 6. Mortality according to left ventricular systolic function and sex in asymptomatic individuals



LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain; MV, mitral valve

eFigure 7. Relationship between left ventricular systolic function and mortality by sex in asymptomatic individuals without evidence of obstructive coronary artery disease
Obstructive CAD was defined as the absence of a history of myocardial infarction and no concomitant CABG.



CABG, coronary artery bypass grafting; CAD, coronary artery disease, LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain