

Supplementary table S1. Univariable and multivariable analyses for MACCE for the sensitivity analysis

	Univariate analysis		Sensitive analysis	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
HFpEF by the HFA-PEFF score	2.56 (1.63 – 4.01)	< 0.001	1.65 (1.03 – 2.64)	0.038
Age	1.09 (1.05 – 1.12)	< 0.001	1.07 (1.04 – 1.10)	< 0.001
Body mass index	0.94 (0.87 – 1.00)	0.058		
Body surface area	0.15 (0.05 – 0.49)	0.002		
Chronic kidney disease \geq grade 3	1.95 (1.25 – 3.04)	0.003		
LV end-diastolic dimension	0.96 (0.91 – 1.01)	0.077		
Moderate or severe TR	2.80 (1.65 – 4.75)	< 0.001	1.83 (1.07 – 3.15)	0.028

Chronic kidney disease is defined as $eGFR < 60 \text{ mL/min/1.73 m}^2$.

CI, confidence interval; *GFR*, glomerular filtration rate; *HFpEF*, heart failure with preserved left ventricular ejection fraction; *HR*, hazard ratio; *TR*, tricuspid regurgitation.

Supplementary table S2. Characteristics and outcome of the study population divided by HFpEF or non-HFpEF in the H₂FPEF score

	HFpEF	Non-HFpEF	P*
	(n = 560)	(n = 1119)	
Demographic data:			
Age, years	75 ± 8	69 ± 11	< 0.001
Sex, male	355 (63.4)	863 (77.1)	< 0.001
Height, m	1.62 ± 0.09	1.67 ± 0.09	< 0.001
Weight, kg	66.1 ± 14.2	65.3 ± 11.3	0.256
Body mass index, kg/m ²	24.9 ± 4.2	23.2 ± 2.9	< 0.001
Body surface area, m ²	1.70 ± 0.20	1.73 ± 0.18	0.003
CHADS ₂ score	2 (1 – 2)	1 (0 – 2)	< 0.001
Congestive heart failure	59 (10.5)	71 (6.3)	0.002
Hypertension	526 (93.9)	399 (35.7)	< 0.001
Age ≥ 75 years	298 (53.2)	366 (32.7)	< 0.001
Diabetes mellitus	112 (19.6)	135 (12.1)	< 0.001
Prior stroke	61 (10.9)	86 (7.7)	0.028
Coronary artery disease	60 (10.8)	82 (7.4)	0.020
Chronic kidney disease ≥ grade 3	23 (41.9)	354 (31.8)	< 0.001
Paroxysmal AF	363 (64.8)	722 (64.5)	0.904

2D echocardiographic data:

LV end-diastolic dimension, mm	46.1 ± 4.6	45.5 ± 4.5	0.010
LVEF, %	62.8 ± 4.0	62.1 ± 4.0	0.001
LV mass index, g/m ²	87.9 ± 17.9	79.6 ± 15.8	< 0.001
LA diameter, mm	40.3 ± 6.4	37.2 ± 6.2	< 0.001
LA volume index, mL/m ²	47.3 ± 14.9	41.3 ± 13.7	< 0.001
LA emptying fraction, %	31.4 ± 14.7	33.1 ± 14.7	0.028
E velocity, cm/s	83.7 ± 19.9	71.3 ± 18.4	< 0.001
Septal e', cm/s	6.8 ± 1.9	8.4 ± 2.3	< 0.001
Lateral e', cm/s	8.8 ± 2.5	10.7 ± 2.9	< 0.001
Mean E/e'	11.3 ± 2.9	7.8 ± 2.4	< 0.001
TRV, m/s (N = 1547)	2.5 ± 0.3	2.3 ± 0.3	< 0.001
Moderate or severe TR	73 (13.1)	88 (7.9)	0.001
Laboratory data:			
BNP, pg/mL (N = 826)	55.4 (33.9 – 123.1)	45.9 (20.6 – 96.2)	< 0.001
NT pro-BNP, pg/mL (N = 942)	280.0 (97.0 – 708.2)	156.2 (56.7 – 538.9)	< 0.001
Estimated GFR, mL/min/1.73 m ²	63.2 ± 14.5	66.9 ± 14.5	< 0.001
HFA-PEFF score	5 (4 – 6)	3 (2 – 4)	< 0.001

Outcome:	6 (6 – 6)	5 (4 – 5)	< 0.001
5-year MACCE			
5-year death	33 (5.9)	44 (3.9)	0.070
5-year hospitalisation for heart failure	19 (3.4)	19 (1.7)	0.028
5-year hospitalisation for stroke	5 (0.9)	6 (0.5)	0.393
5-year AF recurrence	13 (2.3)	21 (1.9)	0.542
	176 (31.4)	318 (28.5)	0.216

Data are expressed as mean \pm SD or median (interquartile range) or number (%).

**P* values refer to the difference between HFpEF and non-HFpEF.

AF, atrial fibrillation; BNP, B-type natriuretic peptide; GFR, glomerular filtration rate; HFpEF, heart failure preserved left ventricular ejection fraction; LA, left atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; MACCE, major adverse cardiovascular and cerebrovascular events; NT pro-BNP, N-terminal prohormone brain natriuretic peptide; TR, tricuspid regurgitation; TRV, tricuspid regurgitation peak velocity.

Okada et al.

Supplementary table S3. Univariable and multivariable analyses for MACCE for the H₂FPEF score

	Univariate analysis		Multivariate analysis 1		Multivariate analysis 2	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
HFpEF by the H ₂ FPEF score	1.53 (0.97 – 2.40)	0.067	1.08 (0.67 – 1.72)	0.759	1.04 (0.65 – 1.67)	0.872
Age	1.09 (1.05 – 1.12)	< 0.001	1.08 (1.05 – 1.12)	< 0.001	1.07 (1.04 – 1.11)	< 0.001
Male	0.73 (0.46 – 1.18)	0.199	0.99 (0.61 – 1.60)	0.952	1.04 (0.64 – 1.70)	0.882
Diabetes mellitus	0.97 (0.51 – 1.83)	0.922			0.94 (0.50 – 1.79)	0.853
Prior stroke	1.57 (0.81 – 3.04)	0.186			1.35 (0.69 – 2.63)	0.381
Chronic kidney disease ≥grade 3	1.95 (1.25 – 3.04)	0.003			1.37 (0.86 – 2.16)	0.183
Moderate or severe TR	2.80 (1.65 – 4.75)	< 0.001			1.94 (1.13 – 3.33)	0.017

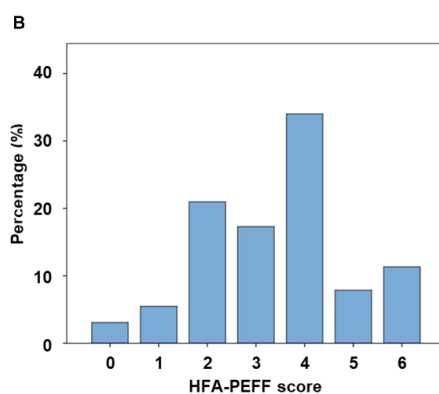
Multivariate analysis model 1 includes HFpEF, age, and sex. Multivariate analysis model 2 includes model 1, hypertension, diabetes mellitus, prior stroke, chronic kidney disease defined as eGFR < 60 mL/min/1.73m², and moderate or severe TR. *CI*, confidence interval; *GFR*, glomerular filtration rate; *HFpEF*, heart failure with preserved left ventricular ejection fraction; *HR*, hazard ratio; *TR*, tricuspid regurgitation.

Okada et al.

Supplementary Figure S1

Description of the HFA-PEFF score (A), and the distribution of the HFA-PEFF score (B) in this study.

A	Functional	Morphological	Biomarker (SR)	Biomarker (AF)
Major criteria: 2 points	E' (sep) <7 cm/s or E'(lat) <10 cm/s or Mean E/e' ≥15 or TRV >2.8 m/s	LAVI >34 mL/m ² or LVMI ≥149/122 g/m ² (M/F) and RWT >0.42	BNP >80 pg/mL or NT-pro-BNP >220 pg/mL	BNP >240 pg/mL or NT-pro-BNP >660 pg/mL
Minor criteria: 1 point	Mean E/e' 9–14	LAVI 29–34 mL/m ² or LVMI >115/95 g/m ² (M/F) or RWT >0.42 or LV wall thickness ≥12 mm	BNP 35–80 pg/mL or NT-pro-BNP 125–220 pg/mL	BNP 105–240 pg/mL or NT-pro-BNP 365–660 pg/mL
HFA-PEFF score ≥5 points: HFpEF (Eur Heart J. 2019; 40: 3297–3317)				



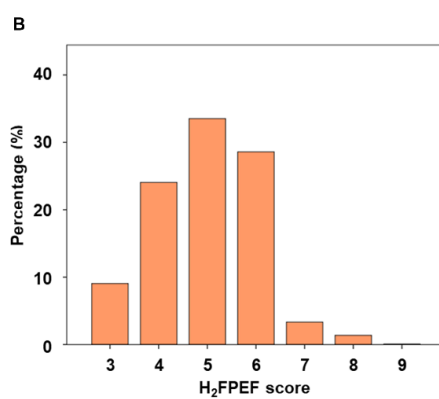
AF, atrial fibrillation; BNP, B-type natriuretic peptide; HFpEF, heart failure preserved left ventricular ejection fraction; LAVI, left atrial volume index; LV, left ventricular; LVMI, left ventricular mass index; RWT, relative wall thickness; TRV, tricuspid regurgitation peak velocity.

Okada et al.

Supplementary Figure S2Description of the H₂FPEF score (A), and the distribution of the H₂FPEF score (B) in this study.

A	Clinical Variable	Values	Points
H2	Heavy	Body mass index >30 kg/m ²	2
	Hypertensive	Hypertension or treatment with two or more anti-hypertensive drugs	1
F	AF	Paroxysmal or Persistent	3
P	Pulmonary Hypertension	TRV >2.8 m/s	1
E	Elder	Age >60 years	1
F	Filling pressure	E/e' ratio >9	1

H₂FPEF score ≥6 points: HFpEF (Circulation. 2018; 138: 861–870)

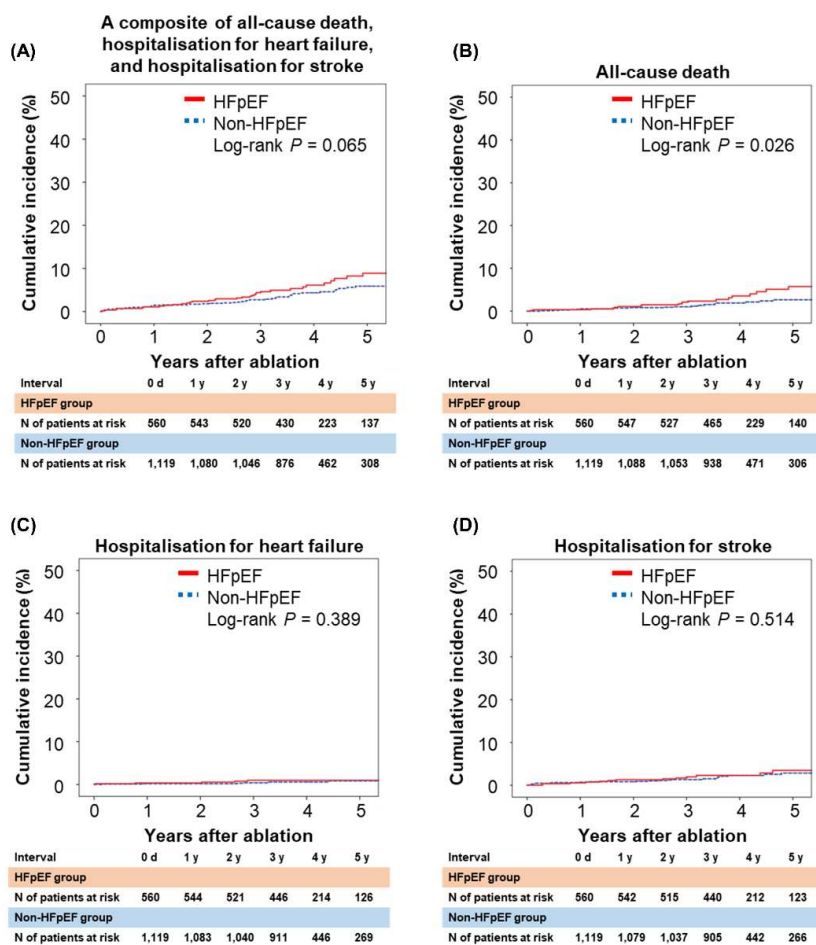


AF, atrial fibrillation; HFpEF, heart failure preserved left ventricular ejection fraction; TRV, tricuspid regurgitation peak velocity.

Okada et al.

Supplementary Figure S3

Kaplan–Meier analyses show the cumulative rate of the primary composite endpoint (A), all-cause death (B), hospitalisation for HF (C), and hospitalisation for stroke (D) stratified by the H₂FPEF score.



HFpEF, heart failure preserved left ventricular ejection fraction.