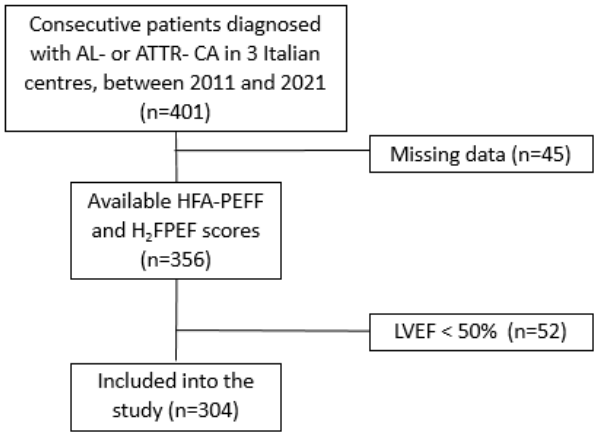
Supplemental material

Supplemental Figure 1. Study flowchart.

AL, immunoglobulin light chain; ATTR, transthyretin; CA, cardiac amyloidosis; LVEF, left ventricular ejection fraction

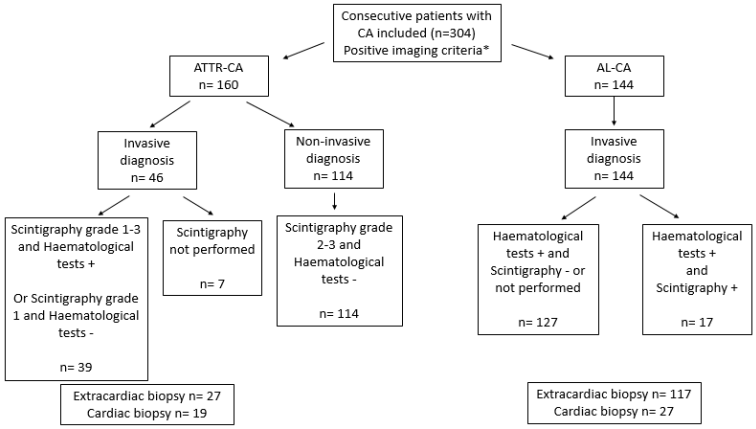


Supplemental Figure 2. Flow chart showing how the diagnosis was confirmed.

AL, immunoglobulin light chain; ATTR, transthyretin; CA, cardiac amyloidosis.

*Imaging criteria refer to echocardiographic findings and cardiac magnetic resonance in a subpopulation of 101 (33%) patients (53 patients with ATTR-CA and 48 patients with AL-CA).

Haematological tests include serum protein electrophoresis with immunofixation; urine protein electrophoresis with immunofixation and serum free light chain assay.



Supplemental figure 3~~2~~. Kaplan Meier curves stratified according to HFA-PEFF scores. Patients with a score of 0-2 were excluded due to the limited number of cases.

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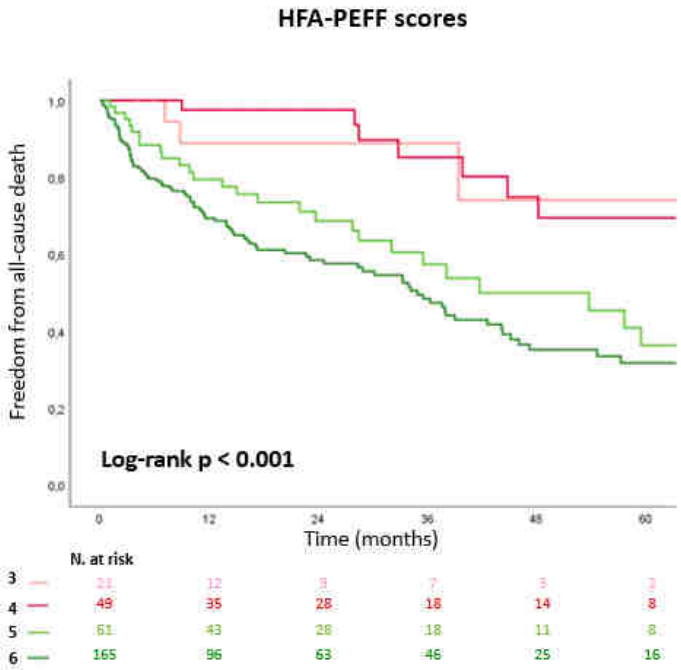
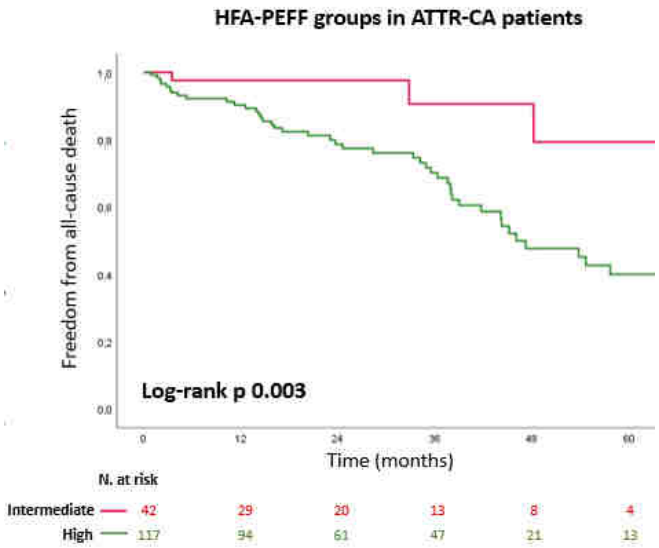
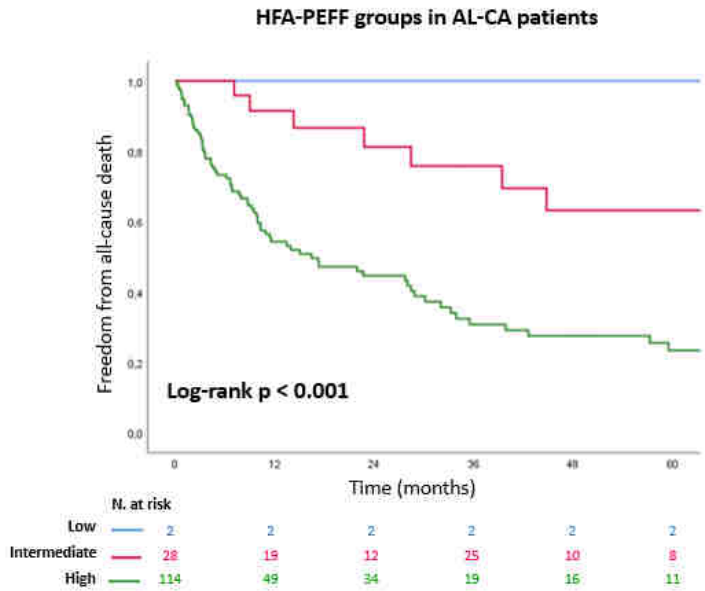

HFA-PEFF scores
Freedom from all-cause death
1,0
0,8
0,6
0,4
0,2
0,0
Log-rank p < 0.001
0
12
24
36
48
60
Time (months)
N. at risk
3 21 12 8 7 3 3
4 49 35 28 18 14 8
5 61 43 28 18 11 8
6 165 96 63 46 25 16

Supplemental figure 43. Kaplan Meier curves stratified according to HFA-PEFF groups in patients with ATTR-CA and AL-CA.

AL, immunoglobulin light chain; ATTR, transthyretin; CA, cardiac amyloidosis





Supplemental table 1. H_2FPEF score calculation.

	Clinical variable	Values	Points
H_2	**H**eavy	Body mass index (BMI) >30 kg/m^2	2
	Hypertension	Treatment with ≥2 antihypertensive drugs	1
F	Atrial **F**ibrillation	Paroxysmal or Persistent	3
P	**P**ulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	**E**lder	Age > 60 years	1
F	**F**illing pressure	Doppler Echocardiographic E/e' >9	1

Supplemental table 2. HFA-PEFF score calculation.

Functional domain – *major criteria*: septal e' <7 cm⁄s, or lateral e′ < 10 cm⁄s [age <75 years]; septal e′ <5 cm⁄s, or lateral e′ <7 cm⁄s [age ≥75 years]; average septal-lateral E⁄e′ ratio ≥15; tricuspid regurgitation peak velocity >2.8m⁄s; PASP >35 mmHg; – *minor criteria*: average septal-lateral E⁄e′ ratio 9-14; LV global longitudinal systolic strain (GLS) <16%.
Morphological domain – *major criteria*: left atrium volume index (LAVI) >34 mL/m^2 in sinus rhythm (SR) or >40 mL⁄m^2 in atrial fibrillation (AF); LV mass index (LVMI) ≥149 g⁄m^2 in men or ≥122 g/m^2 in women plus relative wall thickness (RWT) >0.42 – *minor criteria:* LAVI 29- 34 mL/m^2 in SR or 34-40 mL/m^2 in AF; LVMI ≥115 g⁄m^2 in men or ≥95 g/m^2 in women; RWT > 0.42; LV end-diastolic wall thickness ≥12 mm
Biomarker domain: – *major criteria:* N-terminal of proB-type natriuretic peptide (NT-proBNP) >220 ng/L or B-type natriuretic peptide (BNP) >80 ng/L in SR]; NT-proBNP >660 ng/L or BNP >240 ng/L in AF – *minor criteria:* NT-proBNP 125-220 ng/L, or BNP 35 − 80 ng/L in SR; NT-proBNP 375−660 ng/L, or BNP 105- 240 ng/L in AF.

Supplemental table 3. Univariable analysis for all-cause death

	Univariable	
	HR (95% CI)	*p-value*
Clinical characteristics		
Age at inclusion (years)	1.01 (0.99-1.03)	0.263
Sex (male)	0.82 (0.58-1.17)	0.269
BMI	0.96 (0.91-1.001)	0.057
Type of amyloidosis (AL vs ATTR)	2.11 (1.48-3.00)	<0.001
SBP	0.98 (0.97-0.99)	<0.001
Hypertension	0.87 (0.61-1.23)	0.414
Dyslipidemia	1.09 (0.76-1.56)	0.633
Diabetes	1.37 (0.89-2.09)	0.152
CAD	1.18 (0.76-1.81)	0.469
History of atrial fibrillation	1.29(0.91-1.82)	0.148
Previous HF hospitalization	1.91(1.35-2.70)	<0.001
NYHA class (III-IV vs I-II)	1.40(1.12-1.75)	0.003
Laboratory findings		
Hemoglobin	0.83 (0.75-0.92)	0.001
WBC	1.00(1.00-1.00)	0.833
INR	1.52 (1.18-1.97)	0.001
Lactate dehydrogenase	1.00 (0.99-1.00)	0.401
Cholesterol	0.99(0.99-0.998)	0.002
eGFR	0.98 (0.97-0.99)	<0.001
Log NT-proBNP	3.11 (2.17-4.44)	<0.001
hs-TnT	1.01 (1.01-1.01)	<0.001
Echocardiographic findings		
LVEF	0.99(0.96-1.02)	0.349
IVS	1.03 (0.99-1.08)	0.167
LVPW	105 (1.00-1.11)	0.045
LV-GLS	1.10(1.06-1.15)	<0.001
S' medial	0.84(0.71-0.99)	0.036
S' lateral	0.90 (0.77-1.05)	0.183
E/A	1.26 (1.06-1.49)	0.010
EDT	0.994 (0.990-0.997)	0.001
E/e'	1.07(1.05-1.01)	<0.001
LA diameter	1.02 (0.99-1.05)	0.135
LA area	1.00 (0.997-1.01)	0.257
LAVI	1.02(1.01-1.03)	0.003
RA volume	1..00 (0.99-1.02)	0.694
TAPSE	0.91(0.88-0.95)	<0.001
S'TDI	0.97 (0.91-1.03)	0.276
PASP	1.02(1.01-1.04)	0.004
RV wall thickness	1.17 (0.99-1.38)	0.066
IVC	1.07 (1.03-1.10)	<0.001
Pericardial effusion	1.91(1.35-2.71)	<0.001
Therapy		
ASA	0.805 (0.551-1.177)	0.264
ACEi/ARBs	0.85 (0.60-1.20)	0.364
MRA	1.58 (1.10-2.25)	0.011
Beta-blockers	1.17 (0.82-1.68)	0.388
DOAC	1.01 (0.66-1.53)	0.971
VKA	1.65 (1.09-2.51)	0.019
Furosemide	2.65 (1.68-4.18)	<0.001
Specific therapy	1.26 (0.86-1.86)	0.237
HFpEF scores		
HFA-PEFF	1.57 (1.29-1.93)	<0.001
H_2FPEF	1.10 (1.02-1.20)	0.017

HFA-PEFF group	3.65 (2.04-6.51)	<0.001
H_2FPEF group	1.33 (1.01-1.75)	0.046

Legend: ACEi, angiotensin-converting enzyme-inhibitors; AL, immunoglobulin light chain; ARBs, angiotensin receptor blockers; ASA, acetylsalicylic acid; ATTR, transthyretin; BMI, body mass index; CAD, coronary artery disease; DOAC, direct oral anticoagulants; EDT, E wave deceleration time; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, Heart rate; hs-TnT, high sensitivity troponin T; INR, International Normalized Ratio; IVC, inferior vena cava; IVS, intraventricular septum; LA, left atrium; LAVI, left atrium volume index; LVEF, left ventricular ejection fraction; LV-GLS, left ventricular global longitudinal strain; LVPW left ventricular posterior wall; NYHA, New York Heart Association; NT-proBNP, N-terminal probrain natriuretic peptide; MRA, mineralocorticoid receptor antagonists; PASP, pulmonary artery systolic pressure; RA, right atrium; RV, right ventricular; SBP systolic blood pressure; TAPSE, tricuspid annular plane excursion; TDI, tissue doppler imaging; VKA vitamin K antagonist; WBC, white blood cell count

Supplemental Table 4. Distribution of Mayo stages according to HFA-PEFF score in AL-CA patients.

Variable	All (n=144)	Low HFA-PEFF score (n=2)	Intermediate HFA-PEFF score (n=28)	High HFA-PEFF score (n=114)	P value
Mayo stage					0.004
I	19 (14)	1 (50)	8 (32)	10 (9)	
II	47 (35)	1 (50)	13 (52)	33 (31)	
III	58 (43)	0 (0)	4 (16)	54 (51)	
IV	12 (9)	0 (0)	0 (0)	12 (11)	

Supplemental Table 5. Distribution of Mayo stages according to H_2FPEF score in AL-CA patients.

Variable	All (n=144)	Low H_2FPEF score (n=26)	Intermediate H_2FPEF score (n=99)	High H_2FPEF score (n=19)	P value
Mayo stage					0.016
I	19 (14)	7 (29)	12 (13)	0 (0)	
II	47 (35)	12 (50)	32 (34)	3 (18)	
III	58 (43)	5 (21)	42 (44)	11 (65)	
IV	12 (9)	0 (0)	9 (9)	3 (18)	

Supplemental Table 6. Distribution of Gillmore stages according to HFA-PEFF score in ATTR-CA patients

Variable	All (n=160)	Intermediate HFA-PEFF score (n=43)	High HFA-PEFF score (n=117)	P value
Gillmore stages				0.009
I	53 (33)	16 (37)	37 (32)	
II	69 (43)	24 (56)	45 (38)	
III	38 (24)	3 (7)	35 (30)	

Supplemental Table 7. Distribution of Gillmore stages according to H_2FPEF score in ATTR-CA patients

Variable	All (n=160)	Low H_2FPEF score (n=10)	Intermediate H_2FPEF score (n=80)	High H_2FPEF score (n=70)	P value
Gillmore stages					0.007
I	53 (33)	3 (30)	35 (44)	15 (21)	
II	69 (43)	7 (70)	25 (31)	37 (53)	

III	38 (24)	0 (0)	20 (25)	18 (26)	

Supplemental table 84. Univariable and multivariable Cox regression model in patients with ATTR-CA and AL-CA.

	Univariable		Multivariable	
	HR (95% CI)	*p-value*	HR (95% CI)	*p-value*
ATTR-CA patients				
HFA-PEFF score	1.98 (1.25-3.13)	**0.004**	4.29 (1.93-9.55)	**<0.001**
H_2FPEF score	1.30 (1.10-1.52)	**0.002**	1.17 (0.91-1.49)	0.204
AL-CA patients				
HFA-PEFF score	1.60 (1.27-2.01)	**<0.001**	1.36 (1.02-1.81)	**0.036**
H_2FPEF score	1.19 (1.08-1.32)	**0.001**	0.99 (0.85-1.18)	0.992

Legend: AL, immunoglobulin light chain; ATTR, transthyretin; CA, cardiac amyloidosis; HR, hazard ratio; CI, confidence interval