

Supplemental Material

Table S1. Variable definitions, sources, and use in analyses.

Variable	Definition	Categorization used in multiple imputation and/or subsequent regression models
All-cause death	Death from any cause in the Cause of Death registry. Censored at emigration, 5 years after the index date, or at the end of the study follow-up, i.e. 31st December 2021, whichever came first.	Not used in imputations/logistic regression. In Cox regression models: No; Yes (event indicator), and time until event
Non CV death	Death from any cause in the Cause of Death registry excluded: I, J81, K761, G45, R570. Censored at CV death, emigration, 5 years after the index date, or at the end of the study follow-up, i.e. 31st December 2021, whichever came first.	Not used in imputations/logistic regression. In Cox regression models: No; Yes (event indicator), and time until event
CV death	Underlying CV cause of death in the Cause of Death registry within 5 years after index date (ICD-10 codes: I, J81, K761, R57, G45). Censored at non-CV death/emigration, 5 years after the index date, or at the end of the study follow-up, i.e. 31st December 2021, whichever came first.	Not used in imputations/logistic regression. In Cox regression models: No; Yes (event indicator), and time until event
First HF hospitalisation	Hospitalization diagnosis in the NPR within 5 years after index date (ICD-10 codes: I110, I130, I132, I255, I420, I423, I425-I429, I43, I50, J81, K761, R57). Censored at death/emigration, 5 years after the index date, or at the end of the study follow-up, i.e. 31st December 2021, whichever came first.	Not used in imputations/logistic regression. In Cox regression models: No; Yes (event indicator), and time until event
First all-cause hospitalisation	Hospitalization from any causes in the NPR within 5 years after index date. Censored at death/emigration, 5 years after the index date, or at the end of the study follow-up, i.e. 31st December 2021, whichever came first.	Not used in imputations/logistic regression. In Cox regression models: No; Yes (event indicator), and time until event
Hospitalised at register entry	Variable in SwedeHF	Yes; No
Follow-up type	Variable in SwedeHF	Specialty care; Primary care
Follow-up in nurse-led HF unit	Variable in SwedeHF.	Yes; No
Sex	Variable in SwedeHF.	Male; Female
Age	Variable in SwedeHF.	Not used, but represented in the categorical variable
Age category		<75 years; ≥75 years
Education level	Education from LISA (Statistics Sweden).	University; Secondary; Compulsory school
Income	Variable in Statistics Sweden	Not used but represented in the categorical variable
Income category		≥medium for index year; <medium for index year
With children	Variable in Statistics Sweden	Yes; No
Smoking	Variable in SwedeHF.	No; Yes
NYHA class	Variable in SwedeHF.	Not used, but represented in the categorical variable
NYHA category		NYHA I-II; NYHA III-IV
EF value	Variable in SwedeHF.	Used only in spline model

Body mass index	Variable in SwedeHF.	Not used, but represented in the categorical variable
Body mass index category		<30 kg/m ² ; ≥30 kg/m ²
Mean arterial pressure.	Variables in SwedeHF.	Not used, but represented in the categorical variable
Mean arterial pressure category		<90%; ≥90%
Heart rate	Variable in SwedeHF.	Not used but represented in the categorical variable
Heart rate category		<70%; ≥70%
eGFR	Variable in SwedeHF.	Not used but represented in the categorical variable
eGFR category	Variable in SwedeHF.	≥60ml/min/1.73m ² ; 30-60ml/min/1.73m ² ; ≤30ml/min/1.73m ²
Anaemia	Hemoglobin <120 g/L in women and <130 g/L in men.	No; Yes
NT-proBNP	Variable in SwedeHF.	Not used, but represented in the categorical variable
NT-proBNP category		≥medium for entire cohort; <medium for entire cohort
Peripheral artery disease	Diagnosis in the NPR (ICD-10 codes: I70-I73).	No; Yes
Stroke/TIA	Diagnosis in the NPR (ICD-10 codes: 430-434, 438, I60-I64, I690-I694, G45)	No; Yes
Cancer past 3 years	Diagnosis in the NPR within 3 years prior to the registrations in SwedeHF (ICD-10 codes: C)	No; Yes
Diabetes mellitus	Diagnosis in SwedeHF or in the NPR (ICD-10 codes: E10-E14).	No; Yes
Atrial fibrillation	Atrial fibrillation on ECG or as diagnosis in SwedeHF or in the NPR (ICD-10 code: I48).	No; Yes
Hypertension	Diagnosis in SwedeHF or in the NPR (ICD-10 codes: I10-I15)	No; Yes
COPD	Diagnosis in SwedeHF or in the NPR (ICD-10 codes: J40-J44)	No; Yes
Ischaemic heart disease	Previous coronary revascularisation in SwedeHF, previous myocardial infarction in the NPR, or previous coronary revascularisation in the NPR (ICD-10 codes: 410-414, I20-I25, I252; Procedure codes: FNG, FNA, FNB, FNC, FND, FNE, FNF, FNH).	No; Yes
Valvular disease	Diagnosis in the NPR (ICD-10 codes: I05-I08, I34-I39, Q22, Q230-Q233, Z952-Z954)	No; Yes
Amyloidosis	Diagnosis in the NPR (ICD-10 codes: H401, H409, H402, H408, M663, G560, M480, M488, M438, E85, OP: ACC51, NAG79, ABC56, ABC36)	No; Yes
Aortic stenosis	Diagnosis in the NPR (ICD-10 codes: I350)	Not used in imputation/Cox/logistic regression No; Yes
Hemochromatosis	Diagnosis in the NPR (ICD-10 codes: E831)	Not used in imputation/Cox/logistic regression No; Yes
Hypertrophic cardiomyopathy	Diagnosis in the NPR (ICD-10 codes: I421)	No; Yes

Musculoskeletal disease	Diagnosis in the NPR (ICD-10 codes: M)	No; Yes
Beta-blockers	Variable in SwedeHF.	No; Yes
ACEi/ARB/ARNi (RAASi/ARNi)	Variables in SwedeHF.	No; Yes
MRA	Variables in SwedeHF.	No; Yes
Diuretics	Variable in SwedeHF.	No; Yes
Digoxin	Variable in SwedeHF.	No; Yes
Nitrates	Variable in SwedeHF.	No; Yes
Anticoagulants	Variable in SwedeHF.	No; Yes
Antiplatelets	Variable in SwedeHF.	No; Yes
Statins	Variable in SwedeHF.	No; Yes
HF device category	Device treatment with ICD or CRT in SwedeHF.	No; Yes

Abbreviations: ACEi, Angiotensin-converting enzyme inhibitors; ARB, Angiotensin receptor blockers; ARNi, angiotensin-receptor-neprilysin inhibitor; COPD, Chronic Obstructive Pulmonary Disease; CRT, cardiac resynchronisation therapy; CV, cardiovascular; EF, ejection fraction; eGFR, estimated glomerular filtration rate (calculated by Chronic Kidney Disease Epidemiology Collaboration formula, calculated with the MDRD formula); HF, heart failure; ICD, implantable cardioverter-defibrillator device; ICD-10, International Statistical Classification of Diseases and Related Health Problems - Tenth Revision; LISA, Longitudinal Integrated Database For Health Insurance And Labour Market Studies; MRA, mineralocorticoid receptor antagonist; NPR, National Patient registry; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association functional class; RASi, renin-angiotensin-system inhibitor; SwedeHF, Swedish Heart Failure registry (RiksSvikt); TIA, transient ischemic attack

Table S2. Baseline characteristics according to EF strata

EF	50-54%	55-59%	60-64%	≥65%	p	Missing
n	2,357 (42)	2,039 (37)	881 (16)	299 (5)		
Sociodemographics						
Male	1406 (59.7)	1107 (54.3)	436 (49.5)	128 (42.8)	<0.001	0
Age, years	75 [66, 82]	77 [70, 83]	77 [69, 83]	77 [69, 82]	<0.001	0
≥75 years	1218 (51.7)	1227 (60.2)	520 (59.0)	172 (57.5)	<0.001	0
Education					0.007	1.2
Compulsory school	742 (31.8)	732 (36.4)	288 (33.1)	117 (39.4)		
Secondary school	1033 (44.3)	832 (41.4)	366 (42.1)	128 (43.1)		
University	555 (23.8)	447 (22.2)	215 (24.7)	52 (17.5)		
Income above medium	1237 (52.5)	1009 (49.5)	418 (47.5)	128 (42.8)	0.002	0.1
With children	2009 (85.2)	1725 (84.6)	761 (86.4)	252 (84.3)	0.63	0
Organisational						
Hospitalised	258 (10.9)	313 (15.4)	149 (16.9)	59 (19.7)	<0.001	0
Follow-up in HF unit	1687 (77.1)	1395 (73.9)	555 (67.9)	199 (74.8)	<0.001	7.5
Follow-up in specialty	1425 (63.2)	1144 (58.6)	576 (68.2)	207 (73.9)	<0.001	4.4
Clinical and laboratory variables						
NYHA					<0.001	26.1
I	341 (19.1)	274 (17.8)	106 (17.7)	19 (9.6)		
II	917 (51.4)	743 (48.4)	263 (43.8)	96 (48.7)		
III	515 (28.9)	504 (32.8)	223 (37.2)	79 (40.1)		
IV	12 (0.7)	15 (1.0)	8 (1.3)	3 (1.5)		
NYHA III-IV	527 (29.5)	519 (33.8)	231 (38.5)	82 (41.6)	<0.001	26.1
BMI ≥30 Kg/m ²	528 (33.0)	510 (35.7)	205 (33.6)	88 (40.9)	0.081	30.9
MAP ≥90 mmHg	1216 (55.2)	1105 (57.2)	476 (57.5)	160 (55.7)	0.537	5.9
Heart rate ≥70 bpm	1009 (46.6)	891 (46.8)	379 (46.3)	127 (46.0)	0.993	7.4
GFR, ml/min/1.73m ²					0.013	6.3
≥60	1390 (63.0)	1124 (58.6)	484 (59.1)	155 (54.6)		
30-60	729 (33.1)	705 (36.8)	289 (35.3)	115 (40.5)		
≤30	86 (3.9)	89 (4.6)	46 (5.6)	14 (4.9)		
NT-proBNP, pg/L	1188 [427, 2416]	1390[548, 2715]	1334 [493, 2810]	1,398 [571, 2993]	0.001	21.8
NT-proBNP >median	883 (47.2)	809 (51.9)	361 (51.9)	128 (54.0)	0.015	21.8
Comorbidities						
Diabetes	632 (26.8)	559 (27.4)	235 (26.7)	94 (31.4)	0.385	0
Hypertension	1725 (73.2)	1602 (78.6)	700 (79.5)	246 (82.3)	<0.001	0
IHD	1013 (43.0)	774 (38.0)	326 (37.0)	113 (37.8)	0.001	0
PAD	205 (8.7)	197 (9.7)	60 (6.8)	25 (8.4)	0.096	0
Stroke/TIA	330 (14.0)	328 (16.1)	142 (16.1)	43 (14.4)	0.204	0
AF	1473 (62.5)	1321 (64.8)	577 (65.5)	163 (54.5)	0.002	0
Valvular disease	638 (27.1)	576 (28.2)	269 (30.5)	110 (36.8)	0.003	0
Cancer	329 (14.0)	296 (14.5)	121 (13.7)	43 (14.4)	0.933	0
COPD	274 (11.6)	319 (15.6)	109 (12.4)	38 (12.7)	0.001	0
Musculoskeletal	791 (33.6)	759 (37.2)	335 (38.0)	110 (36.8)	0.03	0

Amyloidosis	239 (10.1)	241 (11.8)	113 (12.8)	40 (13.4)	0.072	0
Aorta stenosis	167 (7.1)	194 (9.5)	91 (10.3)	46 (15.4)	<0.001	0
HCM	10 (0.4)	12 (0.6)	16 (1.8)	25 (8.4)	<0.001	0
Hemochromatosis	10 (0.4)	3 (0.1)	0 (0.0)	0 (0.0)	0.069	0
Anaemia	639 (31.8)	651 (36.9)	255 (33.6)	97 (38.5)	0.005	14.2
Smoking	121 (7.8)	108 (7.7)	40 (7.3)	8 (4.3)	0.398	33.9
Treatments						
BB	2064 (87.6)	1729 (84.8)	717 (81.6)	238 (79.6)	<0.001	0.1
RASi/ARNi	1946 (82.8)	1505 (73.9)	625 (71.2)	202 (67.6)	<0.001	0.3
MRA	1013 (43.1)	767 (37.7)	321 (36.6)	88 (29.4)	<0.001	0.2
Diuretics	1600 (68.0)	1500 (73.7)	617 (70.3)	224 (74.9)	<0.001	0.2
Nitrates	201 (8.5)	180 (8.9)	79 (9.0)	24 (8.0)	0.94	0.2
Antiplatelets	532 (22.6)	423 (20.8)	200 (22.8)	75 (25.1)	0.247	0.2
Anticoagulants	1387 (58.9)	1250 (61.3)	514 (58.5)	142 (47.5)	<0.001	0.1
Statins	1155 (49.1)	957 (47.0)	387 (44.0)	151 (50.5)	0.05	0.2
Digoxin	221 (9.4)	192 (9.4)	98 (11.1)	19 (6.4)	0.102	0.1
CRT/ICD	158 (6.7)	103 (5.1)	28 (3.2)	9 (3.0)	<0.001	0.3

Data are presented as absolute (relative) frequencies, median [interquartile range], and compared by Chi-squared-test and Kruskal Wallis test, respectively.

Abbreviations: AF, atrial fibrillation; ARNi, angiotensin-receptor-neprilysin inhibitor; BB, Betablockers; BMI, Body mass index; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronisation therapy; EF, ejection fraction; eGFR, estimated glomerular filtration rate (calculated by Chronic Kidney Disease Epidemiology Collaboration formula); HCM, hypertrophic cardiomyopathy; HF, heart failure; HR, heart rate; ICD, implantable cardioverter-defibrillator device; IHD, ischemic heart disease; MAP, mean arterial pressure; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association functional class; PAD, peripheral artery disease; RASi, renin-angiotensin-system inhibitor.

Table S3. Association between left ventricular ejection fraction strata with and outcomes

	Crude			Adjusted	
	Event rate	HR (95% CI)	P value	HR (95% CI)	P value
All-cause mortality					
EF 50-54%	86	Ref			
EF 55-59%	106	1.24 (1.09- 1.41)	0.00	1.09(0.93-1.28)	0.29
EF 60-64%	114	1.33 (1.13-1.56)	0.00	1.18(0.96-1.44)	0.12
EF≥65%	116	1.35 (1.06-1.71)	0.02	1.15(0.85-1.55)	0.38
CV mortality					
EF 50-54%	43	Ref			
EF 55-59%	51	1.18(0.98-1.42)	0.09	1.05(0.84-1.31)	0.67
EF 60-64%	53	1.22(0.97-1.54)	0.09	1.05(0.78-1.40)	0.76
EF≥65%	52	1.20(0.84-1.72)	0.31	1.03(0.66-1.59)	0.90
Non-CV mortality					
EF 50-54%	43	Ref			
EF 55-59%	55	1.30(1.08-1.55)	0.01	1.13(0.90-1.42)	0.28
EF 60-64%	61	1.43(1.15-1.78)	0.00	1.32(1-1.76)	0.05
EF≥65%	64	1.49(1.08-2.06)	0.02	1.29(0.86-1.96)	0.22
HFH					
EF 50-54%	74	Ref			
EF 55-59%	85	1.14(0.99-1.31)	0.07	0.94(0.79-1.11)	0.47
EF 60-64%	85	1.14(0.95-1.37)	0.15	0.94(0.76-1.18)	0.61
EF≥65%	86	1.17(0.89-1.54)	0.27	0.83(0.58-1.17)	0.29
All-cause hospitalization					
hospitalization					
EF 50-54%	240	Ref			
EF 55-59%	263	1.09(1.01-1.19)	0.03	0.97(0.88-1.07)	0.58
EF 60-64%	266	1.15(1.04-1.27)	0.00	1.03(0.91-1.17)	0.66
EF>=65%	299	1.38(1.19-1.60)	0.00	1.14(0.94-1.37)	0.18

Outcome analysis assessed by Cox proportional hazards models. Model 1 unadjusted. Model 2 adjusted for all the variables marked with a superscript a (*) in *Table 1*. Results are reported as hazard ratio (HR) with 95% confidence interval (CI). Unadjusted event rates. Events/1000 patient-years

Abbreviations: HFH heart failure hospitalisation

Table S4. Association between left ventricular ejection fraction strata with and outcomes analysis after excluding patients with hypertrophic cardiomyopathy and amyloidosis

	Crude			Adjusted	
	Event rate	HR (95% CI)	P value	HR (95% CI)	P value
All-cause mortality					
EF 50-54%	85	Ref			
EF 55-59%	101	1.19 (1.04- 1.37)	0.01	1.05(0.88-1.24)	0.59
EF 60-64%	113	1.33 (1.11-1.58)	0.00	1.2(0.96-1.5)	0.11
EF≥65%	117	1.38 (1.06-1.80)	0.02	1.11(0.8-1.55)	0.54
CV mortality					
EF 50-54%	42	Ref			
EF 55-59%	46	1.11(0.91-1.36)	0.31	1.03(0.81-1.31)	0.82
EF 60-64%	54	1.29(1.00-1.66)	0.04	1.12(0.82-1.54)	0.48
EF≥65%	60	1.43(0.98-2.07)	0.06	1.2(0.77-1.88)	0.43
Non-CV mortality					
EF 50-54%	43	Ref			
EF 55-59%	55	1.27(1.05-1.54)	0.01	1.07(0.84-1.36)	0.57
EF 60-64%	58	1.36(1.07-1.73)	0.01	1.29(0.95-1.77)	0.1
EF≥65%	58	1.33(0.91-1.94)	0.14	1.01(0.62-1.66)	0.96
HFH					
EF 50-54%	72	Ref			
EF 55-59%	80	1.10(0.94-1.28)	0.25	0.92(0.77-1.11)	0.40
EF 60-64%	80	1.10(0.90-1.35)	0.35	0.94(0.74-1.21)	0.65
EF≥65%	88	1.22(0.90-1.65)	0.20	0.94(0.64-1.36)	0.73
All-cause hospitalization					
hospitalization					
EF 50-54%	233	Ref			
EF 55-59%	255	1.10(1.01-1.19)	0.04	0.98(0.88-1.09)	0.71
EF 60-64%	262	1.15(1.03-1.28)	0.02	1.04(0.9-1.19)	0.61
EF>=65%	289	1.40(1.18-1.65)	0.00	1.17(0.95-1.44)	0.14

Outcome analysis assessed by Cox proportional hazards models. Model 1 unadjusted. Model 2 adjusted for all the variables marked with a superscript a (*) in *Table 1*. Results are reported as hazard ratio (HR) with 95% confidence interval (CI). Unadjusted event rates. Events/1000 patient-years

Abbreviations: HFH heart failure hospitalisation

Figure S1. Flow chart reporting patient selection.

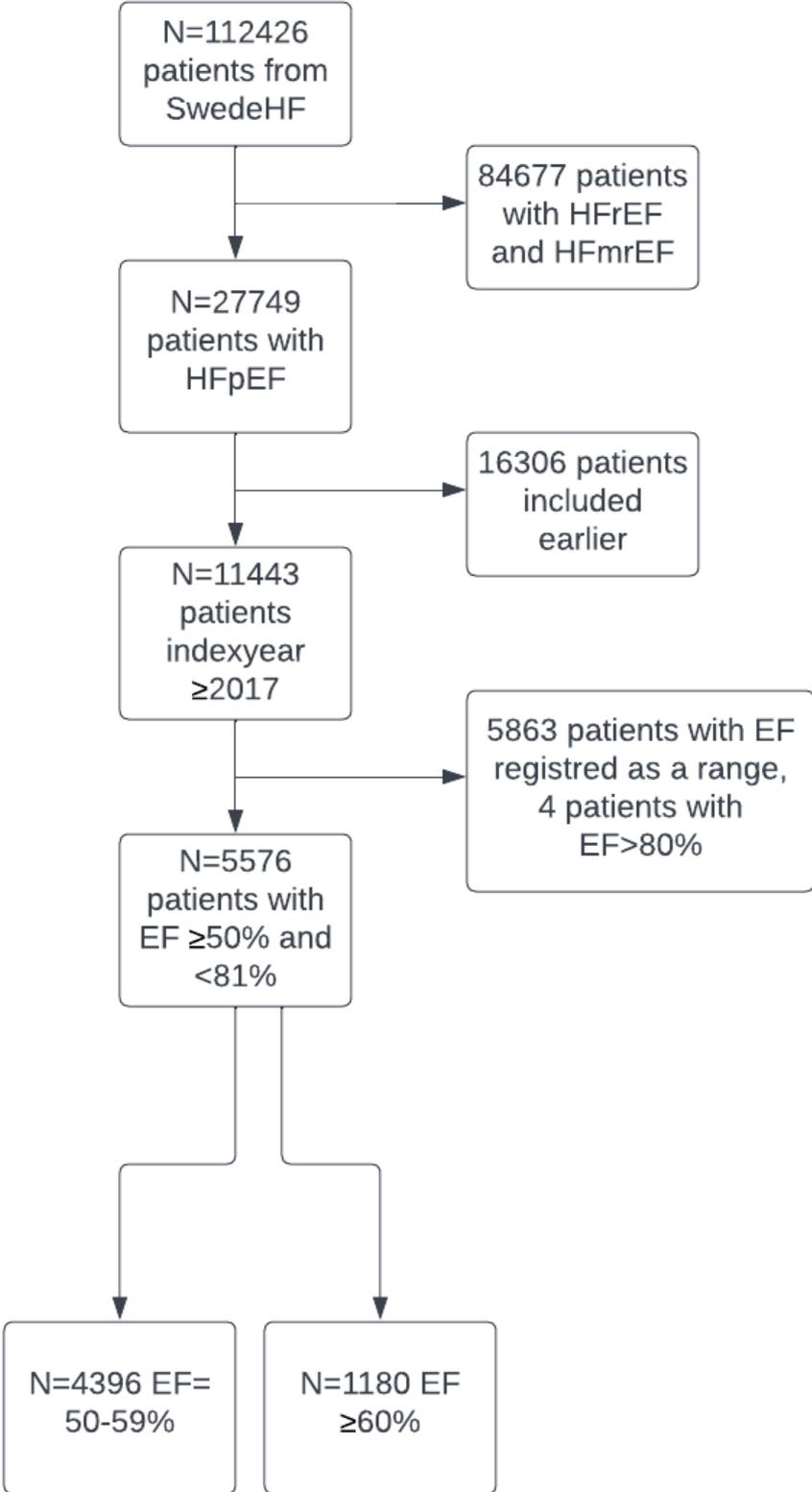
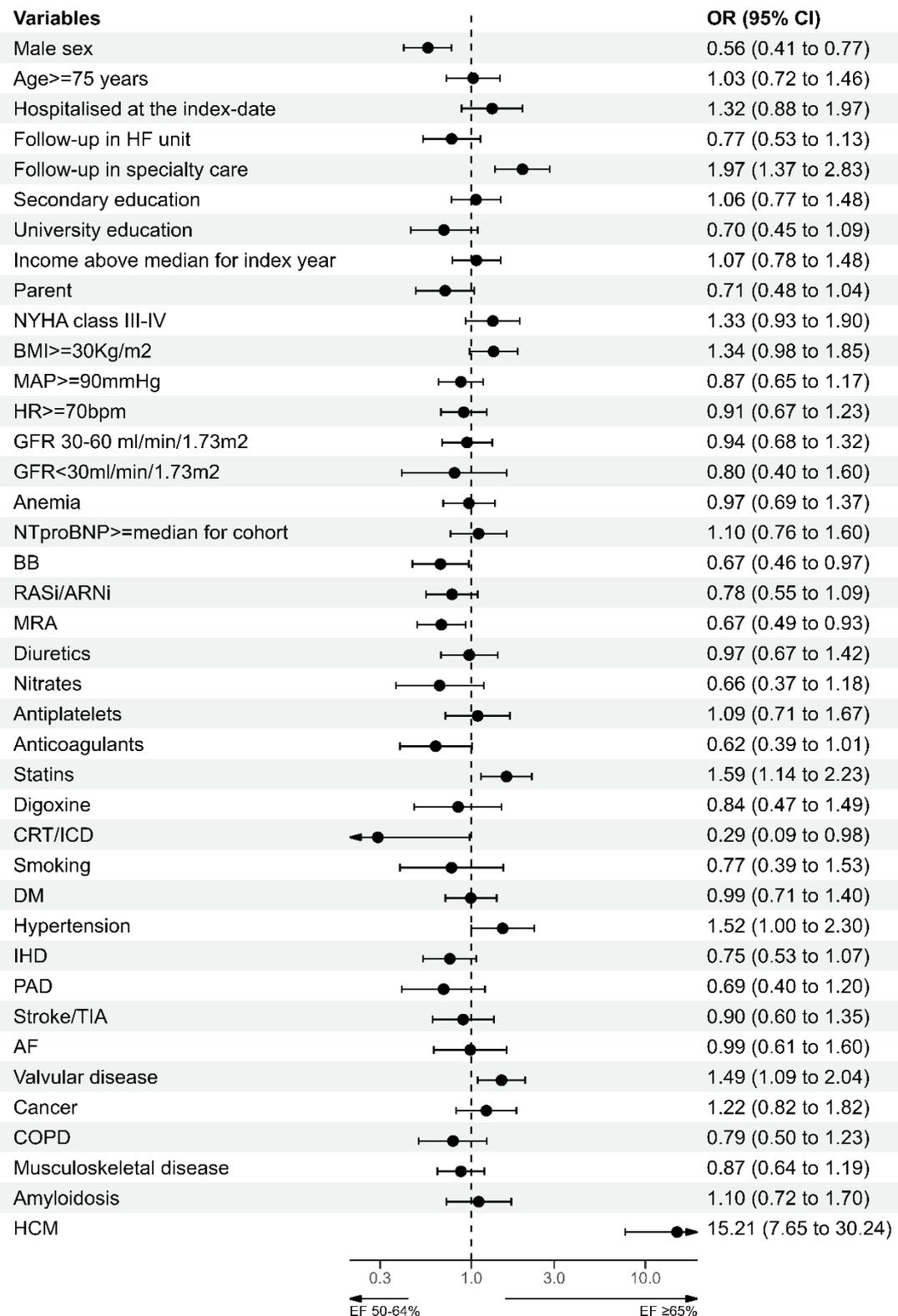


Figure S2. Patient characteristics independently associated with an EF \geq 65% vs EF 50-64%.



Multivariable logistic regression included the variables labelled with * in *Table 1*.

Abbreviations: AF, atrial fibrillation; ARNi, angiotensin-receptor-neprilysin inhibitor; BB, Betablockers; BMI, Body mass index; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronisation therapy; EF,

ejection fraction; eGFR, estimated glomerular filtration rate (calculated by Chronic Kidney Disease Epidemiology Collaboration formula); HCM, hypertrophic cardiomyopathy; HF, heart failure; HR, heart rate; ICD, implantable cardioverter-defibrillator device; IHD, ischemic heart disease; MAP, mean arterial pressure; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association functional class; PAD, peripheral artery disease; RASi, renin–angiotensin-system inhibitor.

Figure S3. Patient characteristics independently associated with an EF $\geq 60\%$ after excluding patients with hypertrophic cardiomyopathy and amyloidosis

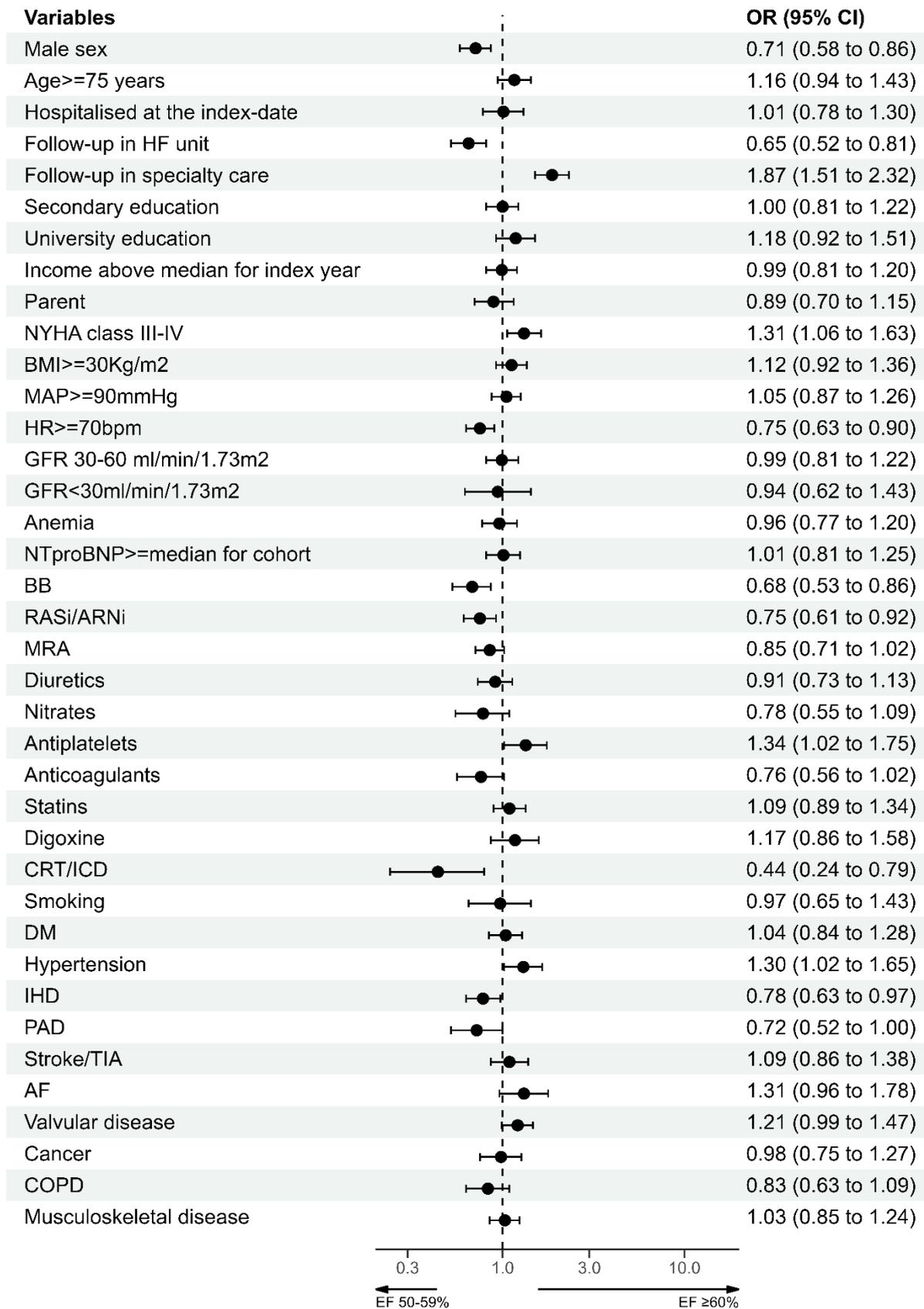


Figure S4. Outcome analysis after excluding patients with hypertrophic cardiomyopathy and amyloidosis

