Supplementary data

METHODS OF THE SUPPLEMENTARY DATA

Definitions

HF diagnoses were obtained from a) the electronic emergency medical record (International Classification of Primary Care, second edition, code K77) or b) the minimum data set (Conjunto Mínimo Básico de Datos, CMBD in Spanish) for hospitalization and emergency care (International Classification of Diseases, 10th Revision (ICD-10) clinical codes I11.0, I13.0, I13.2, and I50*). 1,2 HF was classified according to left ventricular ejection fraction (LVEF), most frequently measured by 2-dimensional echocardiography, in HF with preserved ejection fraction (HFpEF), reduced ejection fraction (HFrEF) and mildly reduced ejection fraction (HFmrEF), with LVEF cutoff points for each group: > 50%, < 40%, and between 41% and 49%, respectively. The eGFR value closest in time to the first ED visit or hospitalization was obtained from the electronic health record (EHR). In the absence of eGFR data, eGFR was calculated using the CKD-EPI formula (mL/min/1.73 m²).^{3,4} Renal function subgroups were defined as normal: eGFR \geq 60; mild renal dysfunction, eGFR 30-59; moderate dysfunction, eGFR 15-29; and severe dysfunction, eGFR <15, which also included patients who were on regular dialysis at the time of the index contact. The indication of dialysis initiation in our hospital follows institutional protocols based on the KDIGO guidelines for acute kidney injury⁵—typically due to refractory fluid overload—and chronic kidney disease.6

ED visits were defined as any medical attention provided in the hospital ED, regardless of time spent or final disposition. The index ED visit was the first visit qualifying for entry to the study. Hospitalization was defined as any hospital stay for any reason lasting beyond

midnight. The index hospitalization was the visit following an admission directly after the first ED visit. Length of hospital stay was calculated as the date of discharge minus the admission date in days.

Follow-up was performed assessing all available data sources. Event rates at 30 days and 365 days after the index ED visit or admission were calculated. Potential states during follow-up included: *a)* death from any cause recorded during the follow-up period; *b)* hospitalization: any hospital stay for any reason after a person was initially discharged from the index ED visit; *c)* readmission: any hospital stay for any reason after a person was discharged from an index hospitalization; *d)* ED revisit: any hospital ED visit for any reason after the initial discharge from the index ED or hospitalization; *e)* outpatient visits were defined as any scheduled medical or nursing consultation in any hospital outpatient facility (specialty visit, day-hospital, HF clinic, cardiac rehabilitation, etc), classified each as first or subsequent; *f)* dialysis: for this particular study, dialysis was registered as a status considering any day when a patient had an outpatient scheduled dialysis session; *g)* days alive out of hospital (DAOH) were defined as those in which patients were alive and in none of the previous states.

The Clinical Outcomes, HEalthcare REsource utilizatioN, and relaTed costs (COHERENT) model

This model was used for the time-dependent analysis of the clinical outcomes, health care resource utilization and cost calculations as recently described.^{7–9} In brief, COHERENT is a model developed for the daily analysis of composite clinical and economic outcomes and health care resource utilization with specific visual outputs. The graphical model is based on the development of a hierarchical code system with a flexible list of mutually exclusive clinical situations defining patient clinical states, which are the combination of vital status (alive or dead) and location (ie, ED, hospital, outpatient facility, dialysis in this particular

case, out of hospital...), which are computed daily during follow-up. The number of clinical situation categories is tailored according to the study's needs. Each clinical state has a daily cost assigned according to local cost estimates. The trajectory of the cohort is represented in area graphs plotting the percentage of patients in each possible clinical situation represented in a set of stacked colored vertical columns on the Y-axis, each column representing 100% of observed patients and each color representing the percentage of patients in each clinical situation, with follow-up days plotted on the X-axis.^{7–9} Graphs were developed with the R Project for Statistical Computing, version 4.0.3 (© 2017 The R Foundation for Statistical Computing, Vienna Austria).¹⁰

Cost calculation

Cost data were obtained from the accountability department of the hospital and were used for estimating the costs of each clinical situation (ie, hospital or ED stays, dialysis sessions). A full cost system in which the cost of each episode was calculated by the addition of all costs imputable to the patient or the episode (housing, diets, drugs, devices) and the unitary costs of each product or activity included in the hospital service catalogue (laboratory analysis, diagnostic and therapeutic interventions, operating room times, postoperative recovery unit stays) was used. All other costs that could not be directly imputed to the patient or the episode (residual cost) were transferred to the clinical episode cost through the indirect imputation criteria. The hospital belongs to the Spanish Network of Hospital Costs (RECH, in Spanish), an initiative that developed a model to calculate the weights and costs of health care processes for patients attended in National Health System hospitals. Daily estimated and cumulative costs were calculated for episodes of care and for the patient journey, including all admissions, ED visits, and day-hospital episodes that a patient with a medical condition experience over the observation time. Total cost distribution and median cost (in euros) per

episode, per patient day and per patient journey were calculated at 30 and 365 days by renal function group.

Table 1 of the supplementary data. International Classification of Diseases 10th Revision (ICD-10) codes used for comorbidities

Risk factors	ICD-10 code
Hypertension	I10, I15.0, I15.1, I15.2, I15.8, I15.9, I16.0, I16.1, I16.9, N26.2
Dyslipidemia	E78, E78.00, E78.01, E78.1, E78.2, E78.3, E78.4, E78.5, E78.6, E78.70, E78.71, E78.72, E78.79, E78.81, E78.89, E78.9
Diabetes	E08*, E09*, E10*, E11*, E13*
Smoking	F17, F17.2, F17.200, F17.201, F17.203, F17.208, F17.209, F17.210, F17.211, F17.213, F17.218, F17.219 F17.220, F17.221, F17.223, F17.228, F17.229, F17.290, F17.291, F17.293, F17.298, F17.299, Z71.6, Z72.0, Z87.891
Comorbidities	
Ischemic heart disease	Q24.0, Q24.1, Q24.2, Q24.3, Q24.4, Q24.5, Q24.6, Q24.8, Q24.9, A52.00, A52.01, A52.02, A52.03, A52.0, A52.05, A52.06, A52.09, A52.10, A52.11, A52.12, A52.13, A52.14, A52.1, A52.16, A52.17, A52.19, A52.2, I25.10, I25.110, I25.111, I25.118, I25.119, I25.2, I25.3, I25.41, I25.42, I25, I25.6, I25.700, I25.701, I25.708, I25.709, I25.710, I25.711, I25.718
Hypertensive cardiopathy	I13.0, I13.10, I13.11, I13.2
Atrial fibrillation	I48.0, I48.1, I4.82, I48.3, I48.4, I48.91, I48.92
Heart valve disease	134.0, 134.1, 134.2, 134.8, 134.9, 135.0, 135.1, 135.2, 135.8, 135.9, 136.0, 136.1, 136.2, 136.8, 136.9, 138, 139
COPD	J41.0, J41.1, J41.8, J42, J43.0, J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, J44.9, J98.2, J98.3
Cancer	C0, C1, C6, C20, C21, C22, C23, C24, C25, C26, C30, C31, C32, C33, C34, C37, C38, C39, C40, C41, C43, C45, C46, C47, C48, C49, C50, C51, C52, C53, C54, C55, C56, C57, C58, C70, C71, C72, C73, C74, C75, C76, C81, C82, C83, C84, C85, C88, C90, C91, C92, C93, C94, C95, C96, C97
Respiratory failure	J96.00, J96.01, J96.02, J96.10, J96.11, J96.12, J96.20, J96.21, J96.22, J96.90, J96.91, J96.92,

COPD, chronic obstructive pulmonary disease; ICD-10, International Classification of Diseases 10th Revision.

Table 2 of the supplementary data. In-hospital medical treatments (drugs prescribed during first hospitalizations)

In-hospital medical therapies	$eGFR \ge 60$ $n = 1197$	eGFR 30-59 n = 1139	eGFR 15-29 n = 333	eGFR < 15 $n = 109$	P	P for trend
HF-related medical treatments						
Beta-blockers	568 (47.5)	583 (51.2)	169 (50.8)	57 (52.3)	.279	.098
Angiotensin-converting-enzyme inhibitors	477 (39.8)	371 (32.6)	63 (18.9)	14 (12.8)	< .001	< .001
Angiotensin II receptor blockers	202 (16.9)	222 (19.5)	41 (12.3)	6 (5.5)	< .001	.014
Angiotensin receptor-neprilysin inhibitors	8 (0.7)	28 (2.5)	4 (1.2)	0 (0.0)	.002	.296
Mineralocorticoid receptor antagonist	234 (19.5)	249 (21.9)	62 (18.6)	5 (4.6)	< .001	.045
Diuretics	1033 (86.3)	1021 (89.6)	302 (90.7)	72 (66.1)	< .001	.113
Other cardiovascular medications						
Aspirin	322 (26.9)	298 (26.2)	84 (25.2)	26 (23.9)	.857	.386
P2Y12 inhibitors	124 (10.4)	110 (9.7)	23 (6.9)	15 (13.8)	.136	.541
Oral anticoagulants	480 (40.1)	557 (48.9)	161 (48.3)	35 (32.1)	< .001	.075
Lipid-lowering drugs	535 (44.7)	557 (48.9)	176 (52.9)	57 (52.3)	.024	.003

eGFR, estimated glomerular filtration rate.

The data are presented as No. (%).

Table 3 of the supplementary data. Rates of in-hospital, 30-day and 1-year clinical outcomes according to renal function in patients with heart failure

	eGFR ≥ 60	eGFR 30-59	eGFR 15-29	eGFR < 15	P	P for
	n = 1453	n = 1327	n = 372	n = 122		trend
30-day mortality	72 (5.0)	106 (8.0)	58 (15.6)	27 (22.1)	< .001	< .001
365-day mortality	296 (20.4)	365 (27.5)	169 (45.4)	48 (39.3)	< .001	< .001
In-hospital mortality	61 (4.2)	95 (7.2)	57 (15.3)	24 (19.7)	< .001	< .001
30-day admissions	1055 (72.6)	993 (74.8)	311 (83.6)	98 (80.3)	< .001	< .001
365-day admissions	1197 (82.4)	1139 (85.8)	333 (89.5)	109 (89.3)	.001	< .001
30-day readmissions	91 (6.3)	100 (7.5)	28 (7.5)	5 (4.1)	.323	.712
365-day readmissions	534 (36.8)	507 (38.2)	173 (46.5)	62 (50.8)	< .001	< .001
30-day ED revisits	188 (12.9)	212 (16.0)	56 (15.1)	13 (10.7)	.081	.387
365-day ED revisits	803 (55.3)	780 (58.8)	212 (57.0)	54 (44.3)	.011	.650

ED, emergency department; eGFR, estimated glomerular filtration rate.

The data are expressed as No. (%).

COHERENT analysis by renal function in patients with HF

Table 4 of the supplementary data. Thirty-day costs per patient journey and episode during the first year according to the level of renal function in patients with heart failure

	eGFR	≥ 60	eGFI	R 30-59	eGFR	15-29	eGFR	< 15	
	Frequencies	Cost (€10³)	Frequencies	Cost (€10³)	Frequencies	Cost (€10³)	Frequencies	Cost (€10³)	<i>P</i> e
Total number of patients	1453	·	1327		372		122		-
Total number of patient-days (30-d)	43 590		39 810		11 160		3660		-
Total cost in euros x 10 ³		5117.2 (100)		5005.1 (100)		1534.6 (100)		610.4 (100)	-
Median cost per patient journey, in € x 10 ³ (Q1-Q3)		2.25 [0.26-4.02]		2.35 [0.81-4.47]		2.79 [1.45-5.77]		3.49 [1.75-6.99]	< .001
Mean cost per patient per day, in euros x 10 ³		0.12 ± 0.34		0.12 ± 0.31		0.13 ± 0.24		0.17 ± 0.37	< .001
Stay by clinical status									
ED mean LOS, d	0.6 ± 0.6		0.7 ± 0.7		0.8 ± 0.7		0.7 ± 0.8		< .001
Hospital mean LOS, d	8.7 ± 9.5		9.1 ± 8.1		10.2 ± 8.6		12.5 ± 10.4		< .001
ED costs									
Total		566.5 (11.1)		540.3 (10.8)		161.7 (10.6)		48.6 (7.9)	-
Index ED visits		495.7 (9.7)		462.7 (9.2)		140.8 (9.2)		43.0 (7.0)	-
ED revisits		70.8 (1.4)		77.6 (1.6)		20.9 (1.4)		5.6 (0.9)	-
Hospitalization costs									-
Total		4518.4 (88.3)		4406.1 (88.0)		1360.3 (88.6)		521.6 (85.5)	-
Index hospitalizations		4260.6 (83.3)		4090.5 (81.7)		1275.1 (83.1)		483.9 (79.3)	-
Internal Medicine		2543.7 (49.7)		2623.8 (52.4)		946.5 (61.7)		384.0 (62.9)	-
Cardiology		1306.6 (25.5)		1142.8 (22.8)		244.0 (15.9)		28.4 (4.7)	-
ICU/CICU		265.1 (5.2)		233.5 (4.7)		31.4 (2.0)		17.8 (2.9)	-
Other		145.2 (2.9)		90.4 (1.8)		53.2 (3.5)		53.7 (8.8)	-
Readmissions		257.8 (5.0)		315.6 (6.3)		85.2 (5.5)		37.7 (6.2)	-
Dialysis		-		-		-		38.3 (6.3)	-
Cost of outpatient care (day hospital)		32.2 (0.6%)		58.6 (1.2)		12.5 (0.8)		1.8 (0.3)	
Median Cost per episode (Q1-Q3)		0.4 [0.4-1.8]		0.4 [0.4-1.9]		0.4 [0.4-2.1]		0.3 [0.1-0.4]	< .001
Cost of events per patient									
Number of episodes	2967		2801		815		477		-
Index ED visits	1453	0.4 [0.1-0.4]	1327	0.4 [0.1-0.4]	372	0.4 [0.4-0.4]	122	0.4 [0.1-0.4]	< .001
ED revisits	282	0.1 [0.1-0.4]	293	0.1 [0.1-0.4]	77	0.1 [0.1-0.4]	20	0.3 [0.1-0.4]	.385
Index hospitalizations	1059	2.3 [1.4-4.1]	1002	2.5 [1.5-4.4]	313	2.6 [1.6-5.3]	99	3.8 [1.8-6.8]	< .001
Readmissions	93	2.0 [1.2-3.2]	106	1.9 [1.1-2.9]	31	1.5 [0.8-2.9]	6	2.8 [2.0-3.2]	.581
Dialysis	-	-	-	-	-	-	226	0.1 [0.1-0.1]	-
Outpatient care (day hospital)	80	0.1 [0.1-0.3]	73	0.3 [0.1-0.4]	22	0.4 [0.3-0.6]	4	0.4 [0.3-0.6]	< .001

CICU, cardiac intensive care unit, ED, emergency department, ICU, intensive care unit, LOS, length of stay.

Values are expressed as median [Q1-Q3] or [P25–P75], mean ± standard deviation, frequencies or total cost (%). All costs are reported in euros (€), with the percentage of each cost relative to the total cost shown in brackets.

Table 5 of the supplementary data. Baseline characteristics according to renal function

-	Т						
	eGFR ≥ 60	eGFR 30-59	eGFR 15-29	eGFR < 15	On Dialysis	P	P-trend
Number of patients	n = 1453	n = 1327	n = 372	n = 87	n = 35		
Female sex	753 (51.8)	790 (59.5)	227 (61.0)	46 (52.9)	11 (31.4)	< .001	.050
Age, y	81.0 [72-86]	85.0 [80-89]	86.0 [80-90]	85.0 [73-88]	71.0 [65-80]	< .001	-
Primary HF diagnosis	905 (62.3)	830 (62.5)	242 (65.1)	48 (55.2)	18 (51.4)	.301	.589
Left ventricular ejection fraction						.313*	-
≥ 50%	969 (66.7)	904 (68.1)	257 (69.1)	64 (73.6)	21 (60.0)		
41-49%	126 (8.7)	106 (8.0)	24 (6.5)	6 (6.9)	5 (14.3)		
≤ 40%	141 (9.7)	148 (11.2)	47 (12.6)	9 (10.3)	7 (20.0)		
Not available	217 (14.9)	169 (12.7)	44 (11.8)	8 (9.2)	2 (5.7)		
Risk factors							
Hypertension	1038 (71.4)	1085 (81.8)	326 (87.6)	68 (78.2)	29 (82.9)	< .001	< .001
Dyslipidemia	768 (52.9)	738 (55.6)	241 (64.8)	44 (50.6)	26 (74.3)	< .001	< .001
Diabetes	578 (39.8)	593 (44.7)	210 (56.5)	48 (55.2)	22 (62.9)	< .001	< .001
Smoking	584 (40.2)	429 (32.3)	128 (34.4)	23 (26.4)	21 (60.0)	< .001	.014
Comorbidities							
Ischemic heart disease	490 (33.7)	504 (38.0)	160 (43.0)	41 (47.1)	16 (45.7)	.001	< .001
Atrial fibrillation	603 (41.6)	700 (52.8)	227 (61.0)	49 (56.3)	12 (34.3)	< .001	< .001
Heart valve disease	480 (33.0)	546 (41.2)	171 (46.0)	43 (49.4)	9 (25.7)	< .001	< .001
COPD	403 (27.7)	293 (22.1)	96 (25.8)	12 (13.8)	9 (25.7)	.001	.006
Cancer	438 (30.1)	407 (30.7)	112 (30.1)	31 (35.6)	16 (45.7)	.290	.175
Respiratory failure	743 (51.1)	708 (53.4)	237 (63.7)	46 (52.9)	23 (65.7)	< .001	< .001

COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; Q1-Q3, first to third quartile interval. The data are expressed as No. (%) or median [Q1-Q3].

^{*} The "on dialysis" group was not included in the tests of hypothesis and associated P values.

COHERENT analysis by renal function in patients with HF

Table 6 of the supplementary data. In-hospital medical treatments (drugs prescribed during first hospitalizations)

In-hospital medical therapies	$eGFR \ge 60$ $n = 1197$	eGFR 30-59 n = 1139	eGFR 15-29 $n = 333$	eGFR < 15 $n = 75$	On dialysis $n = 34$	P	P-trend
HF-related medical treatments							
Beta-blockers	568 (47.5)	583 (51.2)	169 (50.8)	38 (50.7)	19 (55.9)	.389	.095
Angiotensin-converting-enzyme inhibitors	477 (39.8)	371 (32.6)	63 (18.9)	10 (13.3)	4 (11.8)	< .001	< .001
Angiotensin II receptor blockers	202 (16.9)	222 (19.5)	41 (12.3)	4 (5.3)	2 (5.9)	< .001	.010
Angiotensin receptor-neprilysin inhibitors	8 (0.7)	28 (2.5)	4 (1.2)	0 (0.0)	0 (0.0)	.005	.367
Mineralocorticoid receptor antagonist	234 (19.5)	249 (21.9)	62 (18.6)	5 (6.7)	0 (0.0)	< .001	.022
Diuretics	1033 (86.3)	1021 (89.6)	302 (90.7)	59 (78.7)	13 (38.2)	< .001	.008
Other cardiovascular medications							
Aspirin	322 (26.9)	298 (26.2)	84 (25.2)	15 (20.0)	11 (32.4)	.632	.471
P2Y12 inhibitors	124 (10.4)	110 (9.7)	23 (6.9)	6 (8.0)	9 (26.5)	.011	.876
Oral anticoagulants	480 (40.1)	557 (48.9)	161 (48.3)	30 (40.0)	5 (14.7)	< .001	.214
Lipid-lowering drugs	535 (44.7)	557 (48.9)	176 (52.9)	36 (48.0)	21 (61.8)	.025	.002

eGFR, estimated glomerular filtration rate.

Table 7 of the supplementary data. Rates of in-hospital, 30-day and 1-year clinical outcomes according to renal function in patients with heart failure

	eGFR \geq 60	eGFR ≥ 60 eGFR 30-59 eGFR 15-29		eGFR < 15	On Dialysis	P	P-trend
	n = 1453	n = 1327	n = 372	n = 87	n=35		
30-day mortality	72 (5.0)	106 (8.0)	58 (15.6)	25 (28.7)	2 (5.7)	<.001*	<.001
365-day mortality	296 (20.4)	365 (27.5)	169 (45.4)	43 (49.4)	5 (14.3)	< .001	<.001
In-hospital mortality	61 (4.2)	95 (7.2)	57 (15.3)	23 (26.4)	1 (2.9)	<.001*	<.001
30-day admissions	1055 (72.6)	993 (74.8)	311 (83.6)	68 (78.2)	30 (85.7)	< .001	<.001
365-day admissions	1197 (82.4)	1139 (85.8)	333 (89.5)	75 (86.2)	34 (97.1)	.001	<.001
30-day readmissions	91 (6.3)	100 (7.5)	28 (7.5)	2 (2.3)	3 (8.6)	.243	.687
365-day readmissions	534 (36.8)	507 (38.2)	173 (46.5)	33 (37.9)	29 (82.9)	< .001	<.001
30-day ED revisits	188 (12.9)	212 (16.0)	56 (15.1)	9 (10.3)	4 (11.4)	.150	.442
365-day ED revisits	803 (55.3)	780 (58.8)	212 (57.0)	35 (40.2)	19 (54.3)	.010	.641

ED, emergency department; eGFR, estimated glomerular filtration rate.

The data are expressed as No. (%).

^{*} The "on dialysis" group was not included in the tests of hypothesis and associated *P* values.

Table 8 of the supplementary data. One-year costs per patient and episode in heart failure patients according to renal function level

	eG	$FR \ge 60$	eG	FR 30-59	eC	GFR 15-29	e	GFR < 15	(On dialysis	
	Frequencies	Cost (10^3€)	Frequencies	Cost (10^3€)	Frequencies	Cost (10^3€)	Frequencies	Cost (10^3€)	Frequencies	Cost (10^3€)	P
Total number of patients	1453		1327		372		87		35		-
Total number of patient-days	530 345		484 355		135 780		31 755		12 775		-
Total cost, in euros x 10 ³		10 946.9 (100)		10 772.7 (100)		3 672.7 (100)		820.2 (100)		1 355.4 (100)	-
Median cost per patient journey, in euros $x ext{ } 10^3$)		3.96 [1.75-8.41]		4.34 [1.99-10.04]		5.38 [2.41-11.06]		6.88 [2.74-12.73]		32.55 [27.03-48.81]	< .001
Median cost per patient per day, in euros x 10 ³ (SD)		0.02 (0.16)		0.02 (0.16)		0.03 (0.15)		0.02 (0.15)		0.10 (0.39)	< .001
Stays by clinical status											
ED mean LOS, d	0.6 ± 0.7		0.6 ± 0.7		0.7 ± 0.7		0.7 ± 0.8		0.5 ± 0.7		< .001
Hospital mean LOS, d	8.4 ± 8.7		9.0 ± 8.2		10.7 ± 10.7		10.7 ± 8.5		10.5 ± 13.2		< .001
ED costs											
Total		1112.7 (10.2)		1050.4 (9.8)		323.7 (8.8)		66.3 (8.1)		31.0 (2.3)	-
Index ED visits		495.7 (4.5)		462.7 (4.3)		140.8 (3.8)		31.4 (3.8)		12.1 (0.9)	-
ED revisits		616.9 (5.6)		587.7 (5.5)		182.9 (5.0)		34.9 (4.3)		18.9 (1.4)	-
Hospitalization costs											-
Total		9207.1 (84.1)		9365.3 (86.9)		3286.6 (89.5)		740.0 (90.1)		545.3 (40.2)	-
Index hospitalizations		5122.6 (46.8)		4897.3 (45.4)		1456.9 (39.7)		345.2 (42.0)		223.8 (16.5)	-
Internal Medicine		3074.4 (28.1)		3097.4 (28.7)		1064.0 (29.0)		284.6 (34.7)		165.2 (12.2)	-
Cardiology		1604.4 (14.6)		1420.6 (13.2)		285.2 (7.8)		27.5 (3.3)		1.0 (0.1)	-
ICU/CICU		281.1 (2.6)		279.4 (2.6)		31.3 (0.8)		12.3 (1.5)		5.5 (0.4)	-
Other		162.7 (1.5)		100.0 (0.9)		76.4 (2.1)		20.8 (2.5)		52.1 (3.8)	-
Readmissions		4084.5 (37.3)		4468.0 (41.5)		1829.6 (49.8)		394.8 (48.1)		321.5 (23.7)	-
Dialysis		-		-		-		-		700.3 (51.7)	-
Outpatient care (day hospital)		627.1 (5.7)		356.9 (3.3)		62.4 (1.7)		14.5 (1.8)		78.9 (5.8)	-
Median cost per episode		0.4 [0.1-1.4]		0.4 [0.1-1.6]		0.4 [0.3-2.0]		0.4 [0.4-2.3]		0.1 [0.1-0.1]	< .001
Cost of events per patient											
Number of episodes	7056		6289		1820		389		4257		-
Index ED visit	1453	0.4 [0.1-0.4]	1327	0.4 [0.1-0.4]	372	0.4 [0.4-0.4]	87	0.4 [0.3-0.4]	35	0.4 [0.1-0.4]	< .001
ED revisits	2427	01 [0.1-0.4]	2145	0.1 [0.1-0.4]	624	0.4 [0.1-0.4]	119	0.4 [0.1-0.4]	75	0.1 [0.1-0.4]	< .001
Index hospitalizations	1202	2.3 [1.4-4.1]	1149	2.5 [1.5-4.5]	335	2.7 [1.6-5.3]	76	3.1 [1.7-6.6]	34	4.9 [3.3-8.1]	< .001
Readmissions	963	2.5 [1.5-4.3]	975	2.6 [1.5-4.7]	346	2.7 [1.6-5.7]	77	3.2 [1.7-6.5]	50	3.2 [1.8-7.4]	.019
Dialysis	-	-	-	-	-	-	-	-	4038	0.1 [0.1- 0.1]	-
Outpatient care (day hospital)	1011	0.3 [0.1-0.6]	693	0.2 [0.1-0.4]	143	0.3 [0.1-0.5]	30	0.5 [0.3-0.6]	25	3.8 [3.2-4.0]	< .001

CICU, cardiac intensive care unit; ED, emergency department; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; LOS, length of stay; Q1-Q3, first to third quartile interval.

COHERENT analysis by renal function in patients with HF

The data are expressed as median [Q1-Q3] or mean ± standard deviation, as appropriate. All costs are reported in euros (€), with the percentage of each cost relative to the total cost shown in brackets.

Table 9 of the supplementary data. Thirty-day costs per patient journey and episode during the first year according to the level of renal function in patients with heart failure

	eGFR ≥ 60		eG]	FR 30-59	eGl	FR 15-29	eG	FR < 15	On	dialysis	
	Frequencies	Cost (10^3€)	Frequencies	Cost (10^3€)	Frequencies	Cost (10^3€)	Frequencies	Cost (10^3€)	Frequencies	Cost (10^3€)	P
Total number of patients	1453		1327		372		87		35		_
Total number of patient-days (30-d)	43 590		39 810		11 160		2610		1050		-
Total cost in euros x 10 ³		5117.2 (100)		5005.1 (100)		1534.6 (100)		349.0 (100)		261.4 (100)	-
Median cost per patient journey, in euros x 10 ³ (Q1-Q3)		2.25 [0.26-4.02]		2.35 [0.81-4.47]		2.79 [1.45-5.77]		2.83 [0.90-6.46]		6.40 [3.00-8.60]	< .001
Median cost per patient per day, in euros x 10 ³ (SD)		0.12 (0.34)		0.12 (0.31)		0.13 (0.24)		0.13 (0.20)		0.25 (0.62)	< .001
Stay by clinical status											
ED mean LOS, d	0.6 ± 0.6		0.7(0.7)		0.8(0.7)		0.8(0.8)		0.5 (0.6)		< .001
Hospital mean LOS, d	8.7 ± 9.5		9.1 (8.1)		10.2 (8.6)		11.7 (8.1)		14.2 (13.9)		< .001
ED costs											
Total		566.5 (11.1)		540.3 (10.8)		161.7 (10.6)		33.5 (9.7)		15.1 (5.8)	-
Index ED visits		495.7 (9.7)		462.7 (9.2)		140.8 (9.2)		30.9 (8.9)		12.1 (4.6)	-
ED revisits		70.8 (1.4)		77.6 (1.6)		20.9 (1.4)		2.6 (0.8)		3.0 (1.2)	-
Hospitalization costs											-
Total		4518.4 (88.3)		4406.1 (88.0)		1360.3 (88.6)		314.3 (90.0)		207.4 (79.4)	-
Index hospitalizations		4260.6 (83.3)		4090.5 (81.7)		1275.1 (83.1)		310.0 (88.8)		174.0 (66.6)	-
Internal medicine		2543.7 (49.7)		2623.8 (52.4)		946.5 (61.7)		253.4 (72.6)		130.6 (50.0)	-
Cardiology		1306.6 (25.5)		1142.8 (22.8)		244.0 (15.9)		27.5 (7.9)		1.0 (0.4)	-
ICU/CICU		265.1 (5.2)		233.5 (4.7)		31.4 (2.0)		12.3 (3.5)		5.5 (2.1)	-
Other		145.2 (2.9)		90.4 (1.8)		53.2 (3.5)		16.8 (4.8)		36.9 (14.1)	-
Readmissions		257.8 (5.0)		315.6 (6.3)		85.2 (5.5)		4.3 (1.2)		33.4 (12.8)	-
Dialysis		-		-		-		-		38.2 (14.6)	-
Cost of outpatient care (day hospital)		32.2 (0.6)		58.6 (1.2)		12.5 (0.8)		1.2 (0.3)		0.6 (0.2)	-
Median Cost per episode (Q1-Q3)		0.4 [0.4-1.8]		0.4 [0.4-1.9]		0.4 [0.4-2.1]		0.4 [0.4-2.3]		0.1 [0.1-0.3]	< .001
Cost of events per patient											
Number of episodes	2967		2801		815		171		306		-
Index ED visits	1453	0.4 [0.1-0.4]	1327	0.4 [0.1-0.4]	372	0.4 [0.4-0.4]	87	0.4 [0.3-0.4]	35	0.4 [0.1-0.4]	< .001
ED revisits	282	0.1 [0.1-0.4]	293	0.1 [0.1-0.4]	77	0.1 [0.1-0.4]	11	0.1 [0.1-0.4]	9	0.4 [0.1-0.4]	.280
Index hospitalizations	1059	2.3 [1.4-4.1]	1002	2.5 [1.5-4.4]	313	2.6 [1.6-5.3]	69	3.0 [1.7-6.6]	30	4.9 [3.0-7.6]	< .001
Readmissions	93	2.0 [1.2-3.2]	106	1.9 [1.1-2.9]	31	1.5 [0.8-2.9]	2	2.2 [2.0-2.4]	4	3.1 [2.4-9.1]	.719
Dialysis	-	-	-	-	-	-	-	-	226	0.1 [0.1-0.1]	-
Outpatient care (day hospital)	80	0.1 [0.1-0.3]	73	0.3 [0.1-0.4]	22	0.4 [0.3-0.6]	2	0.6 [0.6-0.6]	2	0.3 [0.3-0.3]	< .001

COHERENT analysis by renal function in patients with HF

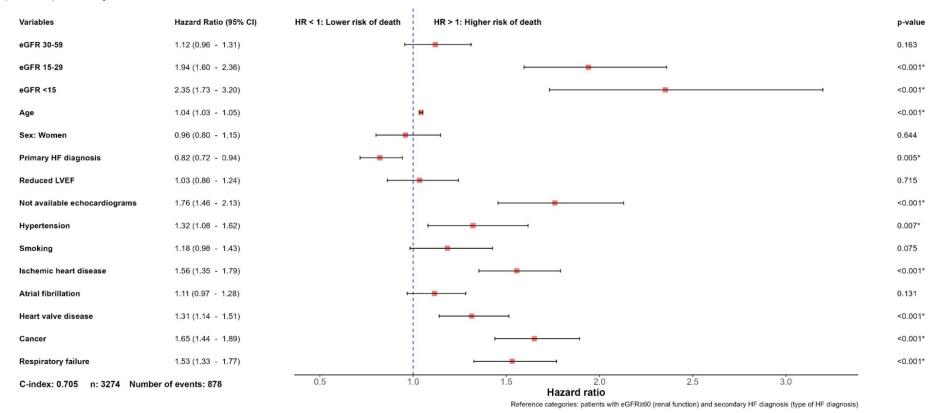
CICU, cardiac intensive care unit; ED, emergency department; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; LOS, length of stay; Q1-Q3, first to third quartile interval

Quantitative variables are expressed as median [Q1-Q3] or mean \pm standard deviation, as appropriate. All costs are reported in euros (\in), with the percentage of each cost relative to the total cost shown in brackets.

.

Figure 1 of the supplementary data. Cox proportional hazards model for 1-year mortality according to the severity of renal function in HF patients

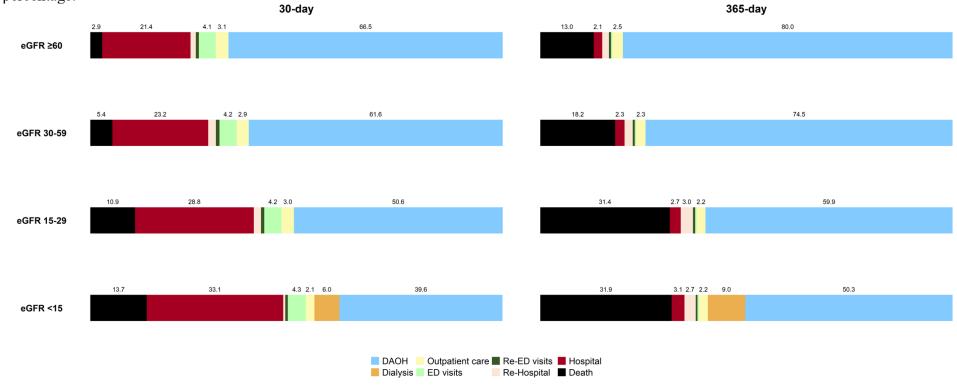
Forest plot showing hazard ratios and 95%CI for variables included in the Cox proportional hazards model. The model evaluates the impact of different severities of renal function (eGFR 30-59, 15-29, and < 15 mL/min/1.73 m²) on mortality in HF patients compared with the eGFR \geq 60 group, adjusted for age, sex, type of HF diagnosis (primary vs secondary), LVEF, risk factors, and comorbidities. The Y-axis lists the covariates, while the X-axis represents the HR. The concordance index, number of observations, and number of events (deaths) are reported.



C-index, concordance index; CI, confidence intervals; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction

Figure 2 of the supplementary data. Proportion of time spent at 30 days (left-hand bars) and 365 days (right-hand bars) according to renal function in heart failure patients.

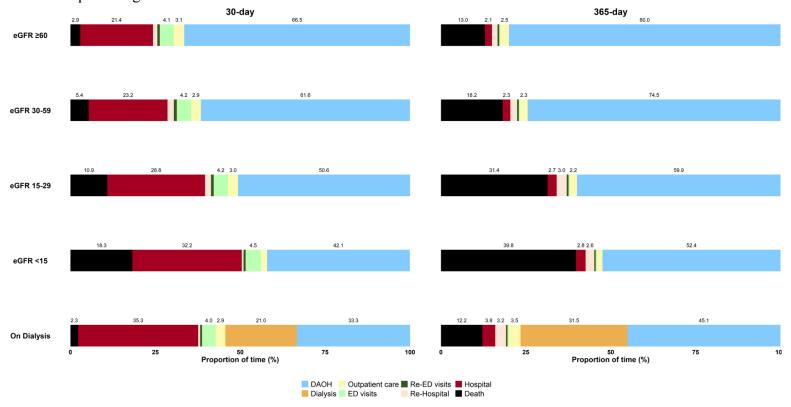
Proportion of time spent in different clinical states (DAOH, outpatient care, ED, hospital, etc) at 30 and 365 days of follow-up in heart failure patients by eGFR. Bar graphs and percentages were derived using the COHERENT model. The X-axis represents the proportion of time as a percentage.



COHERENT, Clinical Outcomes, HEalthcare REsource utilization and relaTed costs; DAOH, days alive out of hospital; ED, emergency department visit; eGFR, estimated glomerular filtration rate; Re-ED, ED revisit: Re-hospital; repeat hospitalization.

Figure 3 of the supplementary data. Proportion of time spent at 30 days (left side bars) and 365 days (right side bars) according to renal function in heart failure patients.

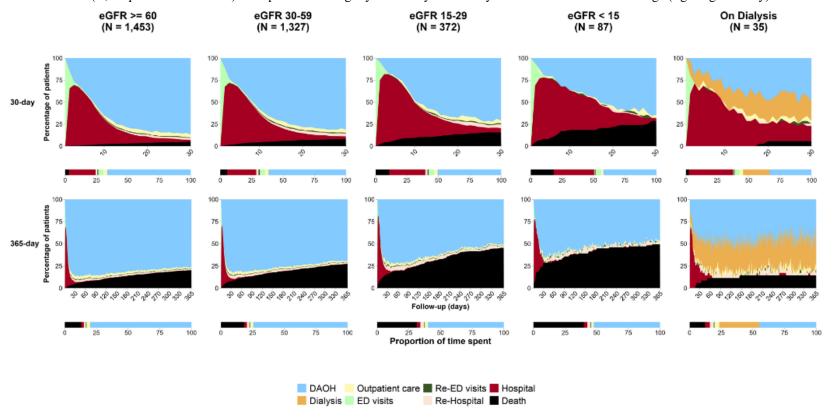
Proportion of time spent in different clinical states (DAOH, outpatient care, ED, hospital, etc.) at 30 and 365 days follow-up in heart failure patients by eGFR and dialysis status. Bar graphs and percentages were derived using the COHERENT model. The X-axis represents the proportion of time as a percentage.



COHERENT, Clinical Outcomes, HEalthcare REsource utilizatioN and relaTed costs; DAOH, days alive out of hospital; ED, emergency department visit; eGFR, estimated glomerular filtration rate; Re-ED, ED revisit; Re-Hospital, repeat hospitalization.

Figure 4 of the supplementary data. COHERENT: 30-day (top) and 1-year (bottom) outcomes by eGFR.

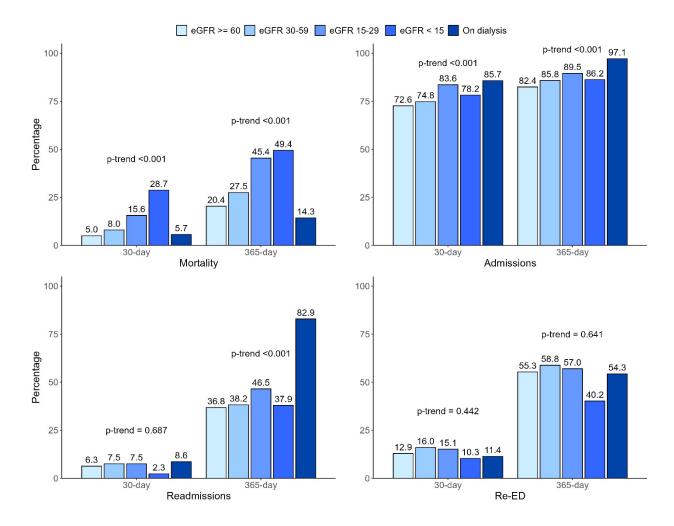
Percentage of patients in each clinical state (Y-axis) on each day during follow-up (X-axis). Light blue areas represent DAOH, light green areas on the left side of the figures represent the time in days spent at the first emergency department visit, brown areas represent the time spent during the first hospitalization. Black areas represent mortality (days deceased). Days in the hospital during readmissions are represented in pink. Days with subsequent stays in the ED are depicted in dark green. Days with any ambulatory care (ie, outpatient office visits) are represented in light yellow. Days with dialysis sessions are shown in orange (right figures only).



COHERENT, Clinical Outcomes, HEalthcare REsource utilization and related costs; DAOH, days alive out of hospital; ED, emergency department visit; eGFR, estimated glomerular filtration rate; Outpatient care, ambulatory care (ie, outpatient office visit); Re-ED, ED revisits; Re-Hospital, repeat hospitalization.

Figure 5 of the supplementary data. Thirty-day and 1-year clinical outcomes by renal function.

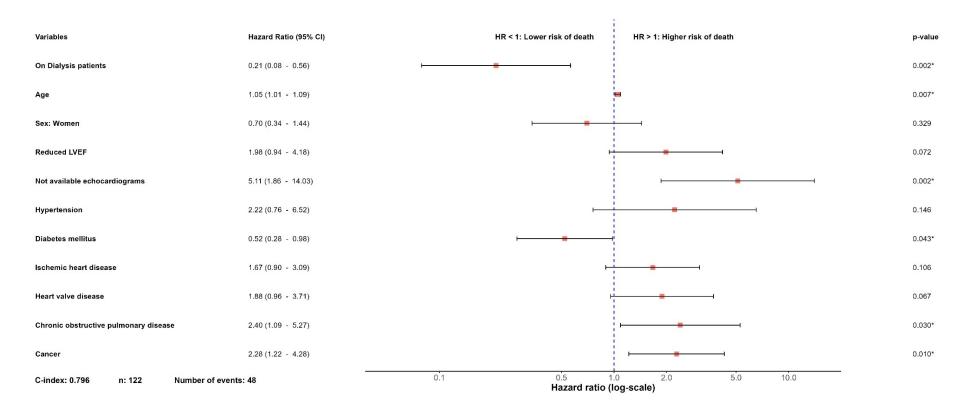
Bar graphs represent the incidence of predefined outcomes (mortality, hospitalizations, readmissions, and new ED visits) at 30 days and 1 year according to renal function, as indicated by estimated glomerular filtration rate or need for dialysis, depicted by progressively darker shades of blue.



ED, emergency department; eGFR, estimated glomerular filtration rate; Re-ED, emergency department revisits.

Figure 6 of the supplementary data. Cox proportional hazards model for 1-year mortality comparing patients with heart failure and $eGFR < 15 \text{ mL/min/1,73 m}^2$ with those on dialysis.

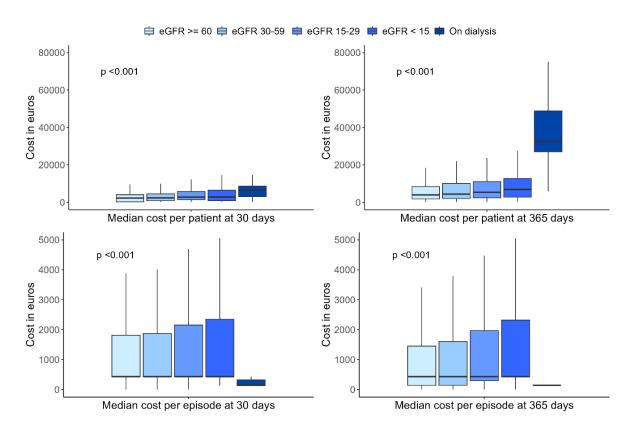
Forest plot showing hazard ratios and 95% CI for variables included in the Cox proportional hazards model. The model evaluates the impact of undergoing dialysis on mortality in HF patients compared with the eGFR < 15 group, adjusted for age, sex, LVEF, risk factors, and comorbidities. The Y-axis lists the covariates, while the X-axis represents the HR on a log scale to enhance clarity. The concordance index, number of observations, and number of events (deaths) are reported.



C-index, concordance index; CI, confidence intervals; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction.

Figure 7 of the supplementary data. Costs per patient (top) and per episode (bottom) by eGFR.

The Y-axis represents costs in euros. The box-and-whisker plots illustrate the median costs (thick central lines inside the box). The lower and upper quartiles (Q1 and Q3) are represented by the lower and upper extremes of the box, and the whiskers represent the minimum and maximum data values. The degree of blue darkness increases with worse renal function, with the darkest blue representing patients on dialysis.



eGFR, estimated glomerular filtration rate.

REFERENCES

- Ministerio de Sanidad. Clasificación Internacional de Enfermedades 10.ª Revisión Modificación Clínica. 2018. Available at:
 https://www.sanidad.gob.es/estadEstudios/estadisticas/normalizacion/CIE10/CIE
 10ES 2018 diag pdf 20180202.pdf. Accessed 28 Mar 2024.
- Ministerio de Sanidad. Clasificación para la explotación conjunta de morbilidad en Atención Primaria. Available at:

 https://www.sanidad.gob.es/estadEstudios/estadisticas/estMinisterio/SIAP/clasif exp morb AP.htm. Accessed 28 Mar 2024.
- 3 Levey AS, Stevens LA, Schmid CH *et al.* A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; **150**: 604–612.
- 4 Bermúdez RM, Bover Sanjuán J, Oliver Samper A, Ballarín Castán JA, Gràcia García S. Valoración de la nueva ecuación CKD-EPI para la estimación del filtrado glomerular. *Nefrología* 2010; **30**: 185–194.
- 5 Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 2012; **120**. doi:10.1159/000339789,.
- Stevens PE, Ahmed SB, Carrero JJ *et al.* KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int* 2024; **105**: S117–S314.
- Bueno H, Bernal JL, Jiménez-Jiménez V *et al.* The Clinical outcomes, healthcare resource utilization, and related costs (COHERENT) model. Application in heart failure patients. *Rev Esp Cardiol (Engl Ed)* 2022; **75**: 585–594.
- Bueno H, Goñi C, Salguero-Bodes R *et al.* Primary vs. Secondary Heart Failure Diagnosis: Differences in Clinical Outcomes, Healthcare Resource Utilization and Cost. *Front Cardiovasc Med* 2022; **9**. doi:10.3389/FCVM.2022.818525/FULL.
- 9 López-Azor JC, Delgado JF, Vélez J *et al*. Differences in clinical outcomes, health care resource utilization and costs in heart failure patients according to left ventricular ejection fraction. *Revista Española de Cardiología (English Edition)* doi:10.1016/j.rec.2023.06.003.
- R: The R Project for Statistical Computing. Available at: https://www.r-project.org/. Accessed 28 Mar 2024.
- Ortega Torres M, del Oro Hitar M, Sastre Barcelo J. Coste GRD: modelo tradicional versus coste por paciente. Hospital Universitario 12 de Octubre. *Gestión y Evaluación de Costes Sanitarios (Fundación Signo)* 2011; **12**.