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Prognostic Factors and Outcomes in Patients Re-Hospitalized for Acute Heart Failure: Insights from a Real-World, Single-Center Retrospective Cohort Study

Facteurs pronostiques et issue vitale chez des patients réhospitalisés pour insuffisance cardiaque aiguë : perspectives issues d'une étude de cohorte rétrospective monocentrique

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Résumé

Contexte et objectif. La mortalité des patients réhospitalisés pour insuffisance cardiaque aiguë (ICA) et les facteurs y associés ne sont pas élucidés. Cette étude visait à déterminer les facteurs pronostiques et l'issue vitale de ces patients. *Méthodes.* Une étude de cohorte rétrospective a été menée au Centre Hospitalier Sud Francilien de janvier 2021 à octobre 2024. Les données des patients réhospitalisés pour une ICA ont été analysées. La régression Cox a été utilisée pour identifier les prédicteurs de mortalité. *Résultats.* Au total, 182 patients (âge moyen 77,6 11,7 ans; 121 (66,5 %) hommes) ont été inclus. La mortalité intrahospitalière était de 41,2 %, avec une survie médiane de 9 jours. L'hypertension artérielle HTA (59,9 %) et le diabète sucré (44,5 %) étaient les facteurs de risque cardiovasculaires (FRCV) les plus fréquents. La fibrillation auriculaire (60,4%) était la principale comorbidité. Les prédicteurs de la mortalité comprenaient l'HTA, le cancer, la bronchopneumopathie chronique obstructive, le passage en soins intensifs, le taux de NT-proBNP >10 000 pg/mL et le taux de CRP ultrasensible ≥ 6 mg/dL. *Conclusion.* Les patients réhospitalisés pour ICA présentent une mortalité intrahospitalière élevée. Celle-ci est déterminée par certains FRCV, certaines comorbidités, l'instabilité hémodynamique et des taux élevés de biomarqueurs du stress pariétal ventriculaire gauche et de l'inflammation systémique. Ces résultats soulignent l'importance de la stratification précoce du risque et de la personnalisation des soins.

Summary

Context and objective. Re-hospitalized acute heart failure (AHF) patients' in-hospital mortality and associated factors are unclear. This study aimed to determine prognostic factors and outcomes in these patients. *Methods.* A retrospective cohort study (January 2021 - October 2024) was conducted at the Centre Hospitalier Sud Francilien. Re-hospitalized AHF patients were analyzed for key data. Cox regression identified mortality predictors. *Results.* A total of 182 patients (mean age 77.6±11.7 years; 121 (66.5%) male) were included. In-hospital mortality was 41.2%, with a median survival of 9 days. Hypertension (59.9%) and diabetes (44.5%) were the most common cardiovascular risk factors (CVRF). Atrial fibrillation (60.4%) was the main comorbidity. Independent mortality predictors included hypertension (HRa=3.76; p=0.001), cancer (HRa=2.84; p=0.014), chronic obstructive pulmonary disease (HRa=2.50; p=0.020), transition to intensive care unit (HRa=3.32; p=0.006), NT-proBNP ≥10,000 pg/mL (HRa=2.02; p=0.008), high-sensitivity C-reactive protein ≥6 mg/dL (HRa=2.25; p=0.018), and cardiogenic shock (HRa=2.36; p=0.005). *Conclusion.* Re-hospitalized AHF patients face a high early mortality. Factors such as specific CVRF, comorbidities, and hemodynamic instability, as well as elevated biomarkers of ventricular wall stress and systemic inflammation are key determinants of in-hospital mortality for these patients. These findings underscore the importance of early risk stratification and individualized care.

Mots-clés : insuffisance cardiaque aiguë, mortalité, re-hospitalisation, survie
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Introduction

Heart failure (HF) is a progressive disease characterized by variable durations of symptomatic stability often punctuated by episodes of worsening despite continued and optimal therapy. These periods of clinical aggravation are increasingly recognized as a distinct phase in the history of HF (1). Episodes of worsening HF are a frequent cause for recurrent hospital readmissions: it has been shown that nearly 1 in 4 patients with acute heart failure (AHF) is readmitted within 30 days of discharge and about half are readmitted within 6 months (2, 3).These episodes are associated with a decrease in quality of life, increased health care costs, and worsening short- and long-term outcomes, including a markedly higher risk of mortality both in-hospital and post-discharge (3).The pathophysiological mechanisms that lead to HF decompensation are intricate, often involving the complex interaction of comorbid conditions, systemic inflammation, neurohormonal dysregulation and hemodynamic instability (4). There have been studies conducted on prognostic factors in patients hospitalized for AHF, with a focus on those who are new-onset heart failure patients. Biomarkers including N-terminal pro B-type natriuretic peptide (NT-proBNP) and C-reactive protein (CRP) have become essential instruments in predicting outcomes in AHF, indicating myocardial stress and systemic inflammation, respectively (6). The presence of comorbidities such as chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), and cancer is widely as a significant factor contributing to increased morbidity and death among HF patients (5-7). However, studies focusing on re-hospitalized AHF patients, a population that is particularly vulnerable and likely to experience poor outcomes, are scarce. It is crucial to understand the demographic, clinical, and biological characteristics that influence prognosis in this setting. This knowledge should be of great importance for timely risk stratification and clinical decision-making to reduce in-hospital mortality and improve survival. By conducting a thorough analysis of readily accessible, including sociodemographic data, comorbidities, clinical presentation, echocardiographic characteristics and biological markers, we aimed to determine prognostic factors and outcomes of re-hospitalized AHF patients.

Methods

Study design and setting

This retrospective analysis of patients' files that were re-hospitalized in the cardiology department of the Centre Hospitalier Sud Francilien (CHSF) located at the junction of Corbeil-Essonnes and Evry, in the department of Essonne in Ile de France.

Patient selection

Inclusion criteria

The study included all men and women aged at least 18 years hospitalized between January 2021 and October 2024 for AHF for the second time,

regardless of the duration between the first hospitalization and the second ongoing hospitalization.

Exclusion criteria:

Patients were excluded from the study if certain data of interest were missing, as well as those who were admitted for post-procedure HF or for a new onset of HF.

Study procedures

All medical records of the selected patients were retrieved and carefully reviewed by two researchers to obtain relevant data on the parameters of interest. These parameters included sociodemographic data, cardiovascular risk factors (CVF), medical history, clinical data, biological data, echocardiographic characteristics, treatment received, duration of hospitalization and vital outcome.

Operational definitions

The following definitions were used in this study:

AHF: in this cohort of re-hospitalized heart failure patients, AHF is defined as an acute decompensation of previously stable chronic heart failure (CHF). It refers to a sudden deterioration in the clinical status of a patient with a known history of CHF, characterized by rapid onset or worsening of signs and symptoms (8). New-onset HF, also known as de novo heart failure, is defined as the sudden or rapid onset of HF symptoms in a patient who previously had no known history of HF (8).

Hypertension was defined as elevated systolic blood pressure (SBP>=140 mmHg) or elevated diastolic blood pressure (DBP>=90 mmHg) and/or taking any antihypertensive medication (9). Diabetes was defined on the basis of the following criteria: fasting glycemia ≥ 7 mmol/L and/or a glycated hemoglobin ≥ 6 5% and/or a personal known history of diabetes mellitus, as per the Consensus Report from the American Diabetes Association (ADA) and European Association for the Study of Diabetes (10). Cigarette smoking was defined as use of any type of smoked tobacco product on a daily or occasional basis (11). Obesity was defined as a BMI greater than or equal to 30 kg/m^2 (12). CKD was defined as decreased kidney function shown by glomerular filtration rate (GFR) of less than 60 mL/min per 1.73 m^2, or markers of kidney damage, or both (13).The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (14). Anemia was defined as a serum hemoglobin concentration of less than 120 g/L for men and less than 110 g/L for women (15). Dyslipidemia was defined as an LDL-cholesterol level ≥ 1.6 g/L and/or an HDL-cholesterol level ≤ 0.40 g/L in men and ≤ 0.50 g/L in women and/or a total cholesterol level ≥ 2 g/L and/or a triglyceride level ≥ 1.5 g/L (16). LDL-cholesterol was calculated using the Friedewald method as LDL-cholesterol (g/L) = CT (g/L) − HDL-cholesterol (g/L) − triglyceride (g/L)/5 (if the triglyceride level was ≤ 3.4 g/L) (16). It was directly dosed using the dextran sulfate filtration technique if the triglyceride level was > 3.4 g/L (16).

Statistical analyses

The information collected was encoded in an Excel database (Microsoft Corporation, USA, 2013) and then imported into the Data Analysis module of SPSS for Windows version 25 for analysis. The results were presented as absolute frequencies (n) and relative frequencies (%), along with central measures (mean and median) and measures of dispersion (SD, IQR). The normality of the distributions was assessed using the Kolmogorov-Smirnov or Shapiro-Wilk test. Mean comparisons were conducted using Student's t-test. If the distributions were not normal, medians were compared using the Mann-Whitney U test. Proportions were compared using Pearson's Chi-square test or Fisher's exact test for numbers less than 5. Patient survival was analyzed using Kaplan Meier curves, and comparisons of these curves were made using the Log rank test. The Cox proportional hazard regression model was utilized to identify predictive factors for mortality. The stepwise method was employed to search for these factors. Only variables that were statistically significant in univariate analysis ($p < 0.05$) were included in the final model. Hazard Ratio (HR) and Adjusted HR (aHR) were calculated to evaluate the risk of association between independent variables and mortality. A significance threshold of $p < 0.05$ was considered for all tests conducted.

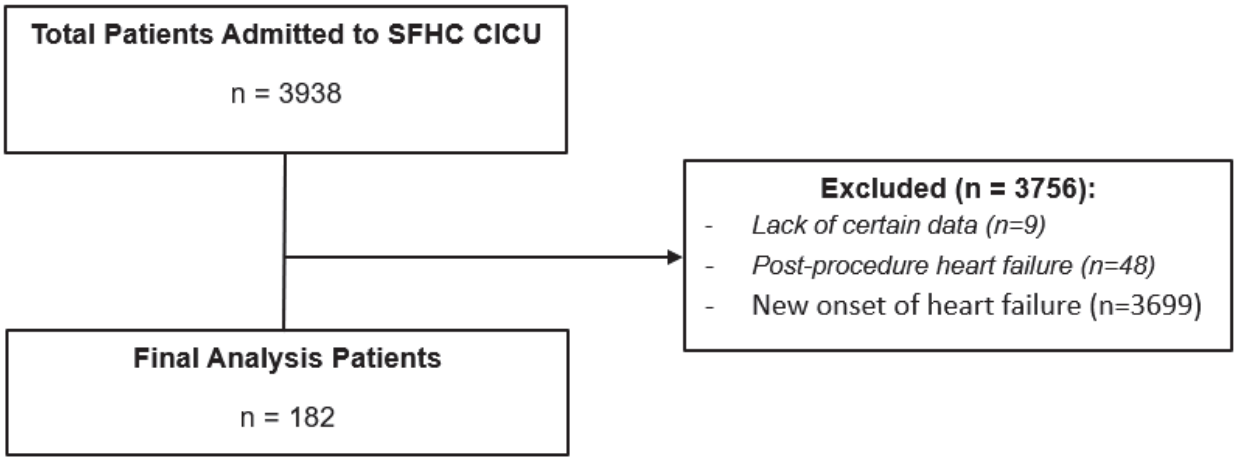
Ethics approval

This study was conducted in accordance with the relevant guidelines and regulations of the Declaration of Helsinki. The data was fully anonymized before being accessed, and the source of the data was patient records.

This study was reviewed and approved by the SFHC Ethics Committee, and all the included patients signed written informed consent.

Results

Of the 3938 HF patients admitted to the SFHC CICU during the study period, 3756 patients were excluded either due to a lack of certain data (n=9) or because they were admitted for post-procedure heart failure (n=48) or a new onset of heart failure (n=3699). A total of 182 patients were selected for the final analysis. Figure 1 summarizes the selection procedure.



SFHC CICU = Sud Francilien Hospital Center Cardiology Intensive Care Unit
Fig 1. Study flow chart

Characteristics of the study population

The study population consisted of 182 patients with a mean age of 77.6±11.7 years. Of these patients, 121(66,5%) were male and 61(33,5%) were female, resulting in a sex ratio of 2.

Socio-demographic characteristics.

Table 1 illustrates the socio-demographic characteristics of the study population based on the vital outcome. The majority of patients studied (52.7%) were aged 80 and over, while those under 65 years of age were a minority (14.3%). There was no statistically significant difference when comparing the vital outcome of patients in different age groups. There were significantly more men among the deceased patients than among the survivors, and significantly more women among the survivors than among the deceased.

Table 1. Socio-demographic characteristics according to mortality

Variables	Whole study population (n=182)	Deceased (n=75)	Survivors (n=107)	p
Sex				0.035
Male	121 (66.5)	56 (74.7)	65 (60.7)	
Female	61(33.5)	19 (25.3)	42 (39.3)	
Mean age	77.6 ± 11.7	78.7 ± 10.8	76.8 ± 12.3	0.262
Age group				0.697
<65 years	26 (14.3)	9 (12.0)	17 (15.9)	
65-79 years	60 (33.0)	24 (32.0)	36 (33.6)	
≥80 years	96 (52.7)	42 (56.0)	54 (50.5)	
Marital status				0.987
Married	108 (59.3)	44 (58.7)	64 (59.8)	
Unmarried	27 (14.8)	12 (16.0)	15 (14.0)	
Widower	37 (20.3)	15 (20.0)	22 (20.6)	
Divorced	10 (5.5)	4 (5.3)	6 (5.6)	

Data are expressed as mean ± standard deviation, absolute (n) and relative (in percent) frequencies

Cardiovascular risk factors, history and comorbidities

Table 2 displays the various cardiovascular risk factors, history and comorbidities of the study population based on survival status.

Hypertension was the most common cardiovascular risk factor (59.9%), followed by diabetes mellitus (44.5%) and obesity (37.4%). With the exception of smoking, which was significantly more common in deceased patients, all other cardiovascular risk factors were present at similar statical proportions between deceased and surviving patients.

Known left ventricular dysfunction, angioplasty, ischemic heart disease, mixed heart disease, and implantable defibrillator, are the history that were found in 114 (77.0%), 80 (44.0%), 55 (32.9%), 41 (24.6%), and 40 (22.0%) patients, respectively.

Present in 110 (60.4%) patients, atrial fibrillation was the most common comorbidity among the patients studied, followed by chronic kidney disease, obstructive sleep apnea syndrome, cancerous disease and chronic obstructive pulmonary disease, present in 61 (33.5%), 36 (19.8%), 28 (15.4%) and 26 (14.3%) patients respectively. Cancer and chronic obstructive pulmonary disease were significantly more common in patients who died during re-hospitalization compared to those who were discharged alive.

Table 2. Cardiovascular risk factors, medical history and comorbidities of the study population based on survival status

Variables	Whole study population (n=182)	Deceased (n=75)	Survivors (n=107)	P value
Cardiovascular risk factors				
Overweight	61 (33.5)	22 (29.3)	39 (36.4)	0.200
Obesity	68 (37.4)	29 (38.7)	39 (36.4)	0.440
Hypertension	109 (59.9)	41 (54.7)	68 (63.6)	0.147
Diabetes	81 (44.5)	31 (41.3)	50 (46.7)	0.285
Dyslipidemia	53 (29.1)	18 (24.0)	35 (32.7)	0.134
Cigarette smoking	52 (28.6)	28 (37.3)	24 (22.4)	0.022
Coronary hereditary	4 (2.2)	1 (1.3)	3 (2.8)	0.453
Medical history				
Heart disease	167 (91.8)	67 (89.3)	100 (93.5)	0.234
Type of heart disease				0.041
Ischemic heart disease	55 (32.9)	30 (44.8)	25 (25.0)	
Hypertensive heart disease	8 (4.8)	1 (1.5)	7 (7.0)	
Cardiomyopathy	26 (15.6)	7 (10.4)	19 (19.0)	
Rhythmic heart disease	26 (15.6)	12 (17.9)	14 (14.0)	
Valvular heart disease	11 (6.6)	3 (4.5)	8 (8.0)	
Mixed heart disease	41 (24.6)	14 (20.9)	27 (27.0)	
Known left ventricular dysfunction	114 (77.0)	49 (77.8)	65 (76.5)	0.506
HFTU	21 (11.5)	5 (6.7)	16 (15.0)	0.066
Angioplasty	80 (44.0)	39 (52.0)	41 (38.3)	0.023
ICD	40 (22.0)	17 (22.7)	23 (21.5)	0.495
Pacemaker	26 (14.3)	13 (17.3)	13 (12.1)	0.220
Prosthetic valve	16 (8.8)	6 (8.0)	10 (9.3)	0.486
Ablation of AF/VT	10 (5.5)	2 (2.7)	8 (7.5)	0.141
Comorbidities				

Atrial fibrillation	110 (60.4)	46 (61.3)	64 (59.8)	0.480
OSA	36 (19.8)	12 (16.0)	24 (22.4)	0.189
COPD	26 (14.3)	15 (20.0)	11 (10.3)	0.032
Cancer	28 (15.4)	18 (24.0)	10 (9.3)	0.007
CKD	61 (33.5)	27 (36.0)	34 (31.8)	0.331

Data are expressed as absolute (n) and relative (in percent) frequencies. HFTU: heart failure therapy unit, ICD: Implantable Cardioverter Defibrillator, AF: atrial fibrillation, VT: ventricular tachycardia, OSA: Obstructive Sleep Apnea, COPD: Chronic obstructive pulmonary disease, CKD: Chornic kidney disease

Clinical and biological data

Table 3 outlines the clinical and biological data of the study population based on vital outcome. Deceased, in comparison to those who survived where more likely to have acute lung edema, be admitted to CICU, and experience desaturation. Additionally, they exhibited significantly lower systolic blood pressure and significantly higher levels of NT-proBNP and hs-CRP.

Table 3. Clinical and biological data of the study population based on vital outcome

Variables	Whole study population (n=182)	Deceased (n=75)	Survivors (n=107)	P value
Clinical type of HF				<0.001
APE	45 (24.7)	26 (34.7)	19 (17.8)	
DHF	133 (73.1)	45 (60.0)	88 (82.2)	
Cardiogenic shock	4 (2.2)	4 (5.3)	0	
Transition to Resuscitation or CICU	48 (26.4)	32 (42.7)	16 (15.0)	<0.001
SBP (mmHg)	125.8 ± 24.0	119.8 ± 25.2	129.9 ± 22.4	0.005
SBP ≥140mmHg	56 (31.1)	18 (24.7)	38 (35.5)	0.083
HR (bpm)	87.4 ± 23.8	90.9 ± 25.4	85.0 ± 22.4	0.100
SpO2	95.1 ± 4.8	94.0 ± 6.0	96.0 ± 3.5	0.009
SpO2<95%	56 (31.6)	29 (40.3)	27 (25.5)	0.015
WBC	6070 (4630-7544)	5000 (1605-8830)	6395 (4630-6940)	0.358
Hs-CRP	16.0 (11.0-54.0)	217.0 (15.0-292.0)	13.5 (5.0-30.0)	0.004
Hs-CRP≥6 mg/dl	115 (76.2)	51 (87.9)	64 (68.8)	0.005
LDL-C	0.56 (0.24-0.74)	0.49 (0.12-1.10)	0.64 (0.37-0.80)	0.495
HDL-C	0.39 (0.28-0.44)	0.28 (0.23-0.700)	0.39 (0.29-0.43)	0.947
Triglycerides	0.78 (0.55-1.07)	1.01(0.23-1.22)	0.64 (0.52-1.07)	0.539
ASAT	34.0 (22.0-85.0)	36.0 (20.0-829.0)	28.5 (19.5-85.0)	0.256
ALAT	28.0 (21.0-82.0)	31.0 (5.0-613.0)	25.0 (19.5-82.0)	0.263
GGT	76.0 (52.0-145.0)	76.0 (52.0-274.0)	71.0 (21.5-113.0)	0.304
ALP	97.0 (76.0-137.0)	103.0 (55.0-262.0)	95.0 (76.0-127.0)	0.968

Data are expressed as mean±standard deviation, absolute (n) and relative (in percent) frequencies, medians with interquartile ranges (IQRs) in parentheses. HF: heart failure, APE: acute pulmonary edema, DHF: Decompensated heart failure, CICU: Cardiac Intensive Care Unit, SBP: systolic blood pressure, HR: heart rat, SpO2: oxygen saturation, WBC: White blood cells, hs-CRP: high-sensitivity C-reactive protein, LDL-C: Low-density lipoprotein-cholesterol, HDL-C: High-density lipoprotein cholesterol, ASAT: aspartate aminotransferase, ALAT: Alanine aminotransferase, GGT: Gamma-glutamyl transpeptidase, ALP: alkaline phosphatase

Echocardiographic data

Table 4 shows the echocardiographic characteristics of the patients included in the study. Aside from the inferior vena cava, which was significantly wider in deceased patients, the other echocardiographic characteristics were statistically similar in both groups.

Table 4. Echocardiographic characteristics of the study population based on vital outcome

Variables	Whole study population (n=182)	Deceased (n=75)	Survivors (n=107)	P
LVEF (%)	40,0 (29,0-54,9)	34,5 (29,0-40,0)	44,0 (32,0-55,0)	0,432
LVEF < 50 %	122 (79,2)	46 (85,2)	76 (76,0)	0,128
LVH	24 (33,3)	7 (29,2)	17 (35,4)	0,399
Kinetic abnormalities	77 (68,8)	26 (72,2)	51 (67,1)	0,375
SPAP (mmHg)	39 (36,1)	15 (40,5)	24 (33,8)	0,314
Valvulopathy	78 (53,1)	30 (55,6)	48 (51,6)	0,386
E/A ration	2,2 (1,9-3,8)	2,0 (1,9-2,1)	2,5 (2,0-3,8)	0,478
E/e' ratio	19,6 (9,0-25,0)	27,0 (20,0-34,0)	15,4 (9,0-20,0)	0,077
TAPSE	18,0 (15,0-21,0)	19,0 (18,0-20,0)	18,0 (13,0-21,0)	0,609
LAV (mm^3)	44,0 (38,0-47,0)	45,0 (44,0-46,0)	41,0 (38,0-47,0)	0,655
IVC (mm)	20,0 (18,0-27,0)	29,5 (27,0-32,0)	20,0 (28,0-20,0)	0,001

Data are expressed as medians with interquartile ranges (IQRs) in parentheses, absolute (n) and relative (in percent) frequencies. LVEF: left ventricular ejection fraction, LVH: left ventricular hypertrophy, SPAP = systolic pulmonary arterial pressure, E/A: ratio of peak early and late diastolic flow velocities, e' : mitral annular early diastolic velocity, TAPSE: Tricuspid annular plane systolic excursion, LAV: left atrium volume, IVC: inferior vena cava.

Vital outcome and overall patient survival

Has depicted in figure 2, re-hospitalization resulted in the deaths of 75 (41.2%) patients.

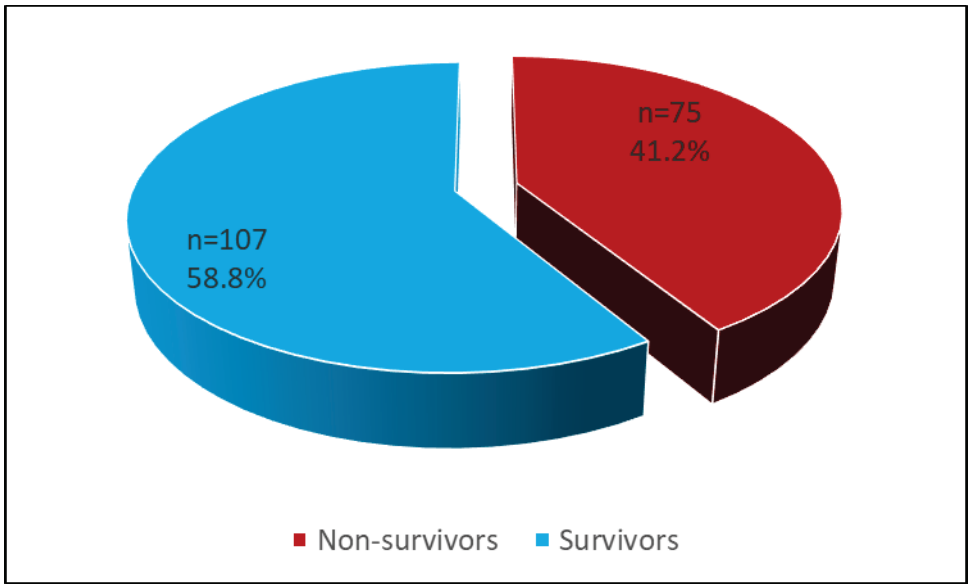


Figure 2. in-hospital death rate

Table 5 reports the various causes of death. Cardiogenic shock, multi-organ failure, and refractory respiratory distress were the primary causes of death, accounting for 10 (13.3%), 17 (22.7%), and 21 (28.0%) of the total deaths, respectively.

Table 5. Causes of death

Causes of death	Deceased

	(n=75)
Refractory respiratory distress	21 (28.0)
Multiple organ failure	17 (22.7)
Cardiogenic shok	10 (13.3)
Rhythm disorder	8 (10.7)
Refractory heart failure	7 (9.3)
hydroelectrolytic disorders	3 (4.0)
Acute renal failure	2 (2.7)
Ischemic Surge	2 (2.7)
None	2 (2.7)
Conduction disorder	1 (1.3)
Valvulopathy	1 (1.3)
Tamponade	1 (1.3)
Total	75 (100.0)

Data are expressed as absolute (n) and relative (in percent) frequencies

Figure 3 highlights the overall survival of patients in the study. The median patient survival was 9.0 days, while the mean was 11 days. This survival varied depending on the length of hospitalization. At seven, fourteen and twenty-one days, it was 85.2%, 64.8%, and 50.6%, respectively. It rose to 43.4% and 41.2% on the thirtieth and fiftieth day of hospitalization.

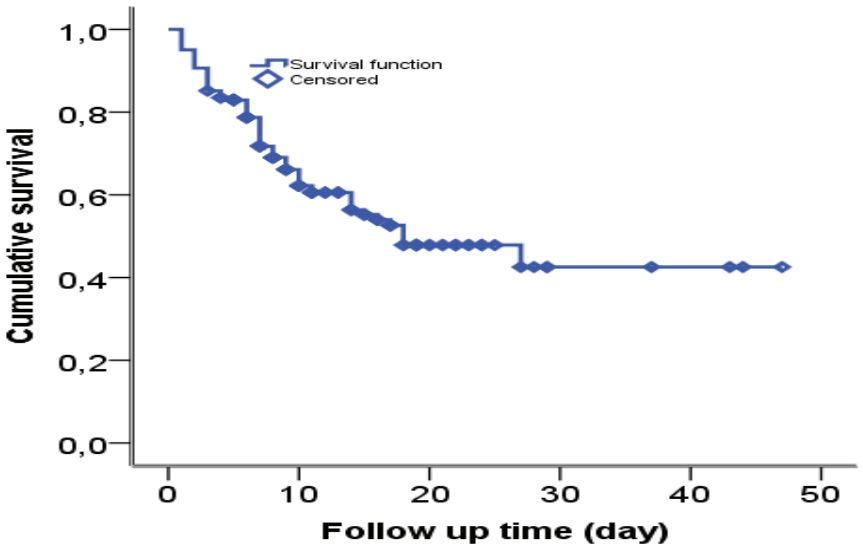


Figure 3. Overall patient survival in the study.

Predictors of mortality

Table 6 depicts the various predictors of mortality. According to Cox's analysis, patients with high blood pressure have a fourfold risk of mortality (HRa=3.76; p=0.001). For patients with chronic obstructive pulmonary disease (COPD) or cancer, the risk of death was approximately three times higher upon re-hospitalization (HRa=2.50; p=0.020, HRa=2.84; p=0.014). Patients with cancer or who had undergone intensive care faced a threefold higher risk of death (HRa=3.32; p=0.006). Individuals with COPD, NTProBNP ≥10,000 pg/ml, cardiogenic shok or hs-CRP ≥ 6 mg/dl had a doubled risk of mortality (HRa=2.50; p=0.020, HRa=2.02; p=0.008, HRa=2.36; p=0.005, HRa=2.25; p=0.018).

Table 6. Predictors of mortality

	Univariate analysis		Multivariate analysis	
Variable	p	HR (CI 95%)	p	aHR (CI 95%)
Sex				
Female		1		1
Men	0.015	1.68 (1.18-2.83)	0.610	1.44 (0.36-5.76)
Hypertension				
No		1		1
Yes	0.016	1.84 (1.18-2.82)	0.001	3.76 (1.65-4.66)
COPD				
No		1		1
Yes	0.022	1.69 (1.41-2.98)	0.020	2.50 (1.51-3.95)
Cancer				
No		1		1
Yes	0.018	1.90 (1.12-3.26)	0.014	2.84 (1.59-4.62)
Angioplasty				
No		1		1
Yes	0.046	1.86 (1.34-2.18)	0.294	1.71(0.63-4.66)
Type of AHF				
DHF		1		1
APE	0.017	2.10 (1.31-3.05)	0.223	1.42 (0.10-1.70)
Cardiogenic shok	0.011	2.53 (1.73-3.86)	0.005	2.36 (1.24-3.98)
Transition to CICU				
No		1		1
Yes	0.000	2.62 (1.66-4.15)	0.006	3.32 (2.84-4.12)
SpO2				
≥95%		1		1
<95%	0.007	1.91 (1.31-2.39)	0.925	1.06 (0.34-3.33)
NT-proBNP				
<10000		1		1
≥10000	0.005	2.02 (1.24-3.29)	0.008	2.02 (1.32-3.23)
Hs-CRP				
<6 mg/dl		1		1
≥6 mg/dl	0.035	2.18 (1.99-4.82)	0.018	2.25 (1.26-3.16)

HR: hazard ratio, aHR: adjusted hazard ratio, COPD: AHF: acute heart failure, DHF: decompensated heart failure, APE: acute pulmonary edema, CICU: Cardiac Intensive Care Unit, SpO2: oxygen saturation, NT-proBNP: N-terminal pro-B-type natriuretic peptide, hs-CRP: high-sensitivity C-reactive protein.

Discussion

This retrospective cohort study aimed to evaluate the prognostic factors and clinical outcomes of patients re-hospitalized for acute heart failure at the Centre Hospitalier Sud Francilien. The main finding of this study is a particularly high hospital mortality rate (41.2%). Hypertension, transition to CICU, cancer, COPD, cardiogenic shok, NT-proBNP level of >10,000 pg/mL, and hs-CRP rate of > 6 mg/dL were the independent factors associated with mortality. Hypertension increased the risk of death fourfold, while transition to CICU and cancer tripled the risk. An NT-proBNP level of >10,000 pg/mL doubled this risk, as did COPD, cardiogenic shok, and a hs-CRP rate of > 6 mg/dL.

In-hospital mortality rate

The in-hospital mortality rate for patients admitted with AHF varies by study and community. A study of 728 consecutive patients treated with AHF found an in-hospital death rate of 8% (17). A study of elderly patients (≥65 years) reported an overall in-hospital mortality rate of 13% (18), with greater rates among those aged ≥85 years. Furthermore, a study of 15,983 patients with congestive HF in intensive care units found an in-hospital mortality rate of 12.4%(19). All of these studies involved patients

hospitalized for AHF, either for primary hospitalization or for readmission. To the best of our knowledge, our study is the first that has specifically focused on patients re-hospitalized for heart failure, a population that is particularly vulnerable. This vulnerability may explain the high mortality rate found in this study.

Demographic and Clinical Characteristics

The average age of the cohort was 77.6 ± 11.7 years, with a majority of elderly patients (52.7% aged ≥80 years), consistent with the well-established epidemiology of heart failure, which primarily affects older adults (20). Interestingly, while there was no statistically significant difference in survival among age groups, a stratified analysis revealed sex-based differences in mortality, with a higher proportion of deceased patients being male. This aligns with previous research indicating that male HF patients often have worse short-term outcomes compared to females (21, 22). Several factors may contribute to this disparity. Men typically have a higher prevalence of ischemic heart disease and more severe left ventricular dysfunction, both which are associated with a poorer prognosis (23). Additionally, sex-related differences in symptom perception, disease progression, and response to therapy may also play a role. On the other hand, women with heart failure are more likely to present with preserved ejection fraction and exhibit a more favorable response to certain therapies, potentially contributing to their lower observed mortality (24). However, despite better survival rates, and after controlling for age, ejection fraction, and New York Heart Association classification, women often report lower quality of life and higher rates of functional impairment. This indicates that survival advantages may not fully reflect the burden of the disease (25).

Cardiovascular Risk Factors and Comorbidities

Hypertension (59.9%) and diabetes mellitus (44.5%) were the most prevalent cardiovascular risk factors, in line with global data that links these conditions to the development and progression of heart failure (26, 27). Interestingly, while most risk factors showed no significant differences between survivors and non-survivors, smoking was more common among those who did not survive, highlighting its well-known contribution to cardiovascular morbidity and mortality [4]. A systematic review and meta-analysis found that persistent smoking increased the hazard ratio of mortality by 38.4% (HR=1.384; 95% CI: 1.139–1.681(28). Therefore, smoking cessation programs are an essential component of care for patients with HF(29).

Comorbidities such as AF (60.4%), CKD (33.5%), COPD (14.3%), and cancer (15.4%) were highly prevalent.

The prevalence of AF found in this study is one of the highest ever reported. A recent systematic review and meta-analysis reported a frequency ranging from 32% to 43% according to heart failure subtypes (HFrEF, HFmEF, HFpEF) (30). Studies have shown that the prevalence of AF in heart failure patients rose as the disease's severity increased, from 5% in mild heart failure patients to 10% and 26% in intermediate heart failure patients to 50% in severe heart failure patients (31). The high prevalence found in this study may be due to the severity of their heart failure as suggested by the very high average NT-pro-NBN rate.

Heart failure (HF) and chronic kidney disease (CKD) often coexist (6, 32, 33). The pathophysiology of this association is complex, multifactorial, dynamic, and bidirectional. Common mechanisms leading to the dysfunction of these organs create a vicious cycle of cardiorenal deterioration (32, 33). A meta-analysis found 32% of HF patients also having CKD (34), a prevalence similar to that found in this study.

COPD and HF coexist so frequently that this couple has been designated as "partners in crime" (35). In sub-Saharan Africa, the prevalence of COPD in heart failure patients is a significant concern, with studies indicating a high burden of COPD in this region(36) . The results of the INTER-CHF study indicate a frequency ranging from 25.2% to 47.5% in this region (37). The reported prevalence of COPD ranges from 11% to 52% in North American patients with HF, and from 9% to 41% in European cohorts(38). The frequency of COPD found in this cohort of heart failure patients falls within these ranges.

The finding of cancer as prevalent comorbidity among HF patients in this study is in line with a previous study which has shown that HF patients are at an increased risk of incident cancer(39). Details of the type, site, and stage of cancer were unavailable in the dataset. The significant association between cancer or COPD and in-hospital mortality is consistent with prior studies demonstrating the additive burden of these comorbidities on heart failure outcomes (35, 38,

39). Multivariate Cox regression confirmed this association, with COPD and cancer doubling and tripling the risk of death during re-hospitalization, respectively. These findings underscore the importance of integrated, multidisciplinary management strategies for patients with multimorbidity.

Prognostic Indicators and Biomarkers

Patients who died were more likely to present with acute pulmonary edema, desaturation, and transition to the CICU, all of which are indicative of hemodynamic and respiratory instability. Additionally, lower systolic blood pressure and elevated biomarkers, NT-proBNP and CRP, were independently associated with mortality. Elevated NT-proBNP reflects increased ventricular wall stress, while CRP is a marker of systemic inflammation, both of which are known predictors of adverse outcomes in heart failure (40-42).

The identified threshold of NT-proBNP ≥10,000 pg/mL and CRP ≥6 mg/dL conferring a doubled mortality risk reinforces their prognostic value and supports their use for early risk stratification. Importantly, ICU admission itself was a strong predictor of mortality (HRa=3.32), potentially reflecting the advanced disease stage or delayed presentation in this subgroup.

Survival Analysis and Timing of Mortality

The median survival of only 9 days post-admission underscores the severity of re-hospitalized AHF. Survival rates declined sharply by the 30th day (43.4%), illustrating a steep early mortality risk. Leading causes of death, including refractory respiratory distress, multi-organ failure, and cardiogenic shock, highlight the need for prompt identification and aggressive management of decompensation. These causes align with known pathways of mortality in AHF (43).

Moreover, the fourfold mortality risk associated with hypertension (HRa=3.76) is clinically relevant and is in line with previous studies depicting that hypertension significantly contributes to in-hospital mortality in HF patients. Studies show mortality rates ranging from 3.8% to 11% for acute heart failure (AHF) and higher rates in intensive care unit (ICU) settings (44).

Implications for Clinical Practice and Research

This study identifies several high-risk profiles that could benefit from targeted interventions:

- Patients with COPD or cancer may require anticipatory palliative care involvement.
- Those with high NT-proBNP or CRP on admission should be considered for closer hemodynamic monitoring or advanced therapies.
- ICU-level care should trigger multidisciplinary review to optimize outcomes and potentially guide decisions on escalation versus palliation.
- Patients with COPD or hypertension should receive special attention.

Strengths and Limitations

A major strength of this study lies in its real-world dataset, spanning nearly four years and reflecting actual clinical practice. However, its retrospective design limits causal inference, and residual confounding cannot be excluded. Biomarker data were available only for hospitalized patients, and outpatient follow-up or functional status prior to re-hospitalization was not assessed. Additionally, details such as the type, site, and stage of cancer were missing from the dataset, leading to a lack of precision and uncertainty. Furthermore, since this is a single-center study, the findings may not be generalizable to other populations or healthcare systems.

Conclusion

Patients who are re-hospitalized with AHF are at a particularly high risk for early mortality. Key predictors of this risk include COPD, cancer, hypertension, CICU admission, and elevated levels of NT-proBNP and hs-CRP. These findings emphasize the importance of early risk assessment and can guide more personalized and proactive management strategies to enhance survival rates in this vulnerable population.

Conflict of interest

The authors declared that they have any conflict of interest.

Contribution for authors

AEEA and BKP wrote the first draft of the manuscript; AEEA and ANN prepared the database; ANN carried out the statistical analyses; AEEA, FNN, YSM, BMM, GIM, JMMM, YMD, CKM, YMV, YLN, TMS, PG, ANN, FNM, and BKP have read and revised manuscript; BKP was scientific coordinator of the work.

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