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In-Hospital Survival and Mortality Predictors of Acute Heart Failure Patients: Insights from a Real-World Single-Center retrospective cohort study

Survie et prédicteurs de la mortalité intrahospitalière des patients avec d'insuffisance cardiaque aiguë : Perspectives issues d'une cohorte rétrospective monocentrique

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Résumé

Contexte et objectif. L'insuffisance cardiaque aiguë (ICA) demeure une cause majeure d'hospitalisation et de mortalité. Cette étude visait à identifier les prédicteurs indépendants de la mortalité hospitalière chez les patients admis pour ICA. *Méthodes***.** Une analyse rétrospective a été réalisée entre janvier et juin 2022 au Centre Hospitalier Sud Francilien, à Corbeil (France). Les données démographiques, cliniques, biologiques et échocardiographiques ont été comparées selon le statut vital à la sortie. L'analyse de survie de Kaplan-Meier et la régression de Cox ont permis d'identifier les facteurs associés à la mortalité. *Résultats.* Les données de 293 patients âgés de 72.4 ± 12.5 ans ont été analysées. La mortalité hospitalière était de 9,6 %, avec une durée médiane de séjour de 8 jours. Une survie significativement réduite a été observée chez les patients atteints de fibrillation auriculaire, de cancer, d'insuffisance rénale chronique (IRC) et de choc cardiogénique. L'hypertension, le cancer, l'IRC, l'anémie, le taux de NT-proBNP ≥10 000 pg/ml, la dysfonction ventriculaire droite et le choc cardiogénique étaient indépendamment associés à la mortalité. *Conclusion.* La mortalité hospitalière liée à l'ICA résulte de comorbidités sévères et d'altérations hémodynamiques. La détection précoce des patients à haut risque est essentielle pour optimiser les interventions thérapeutiques.

Summary

*Context and objective***.** Acute heart failure (AHF) is a leading cause of hospitalization and in-hospital mortality. The objective of the study was to determine predictors of in-hospital mortality among AHF patients. *Methods.* in this retrospective cohort study, demographic, clinical, biological, and echocardiographic characteristics of AHF patients were analyzed at the Centre Hospitalier Sud Francilien in Corbeil, France. Cox proportional hazards models were used to identify independent predictors of in-hospital mortality. *Results.* Data from 293 patients aged 72.4 ± 12.5 years were analyzed. The in-hospital mortality rate was 9.6%. Median hospital stay was 8 days. Kaplan-Meier survival analysis revealed significantly lower survival rates in patients with atrial fibrillation (p = 0.011), cancer (p = 0.006), CKD (p = 0.042), and cardiogenic shock (p < 0.001). In multivariate analysis, hypertension (AHR = 2.39), cancer (AHR = 2.10), CKD (AHR = 2.64), anemia (AHR = 2.59), NT-proBNP levels ≥10,000 pg/ml (AHR = 3.00), right ventricular dysfunction (AHR = 3.52), and cardiogenic shock (AHR = 4.74) were independently associated with mortality. *Conclusion.* In-hospital mortality in AHF is influenced by a combination of comorbidities, cardiac dysfunction, and hemodynamic compromise. Early detection of high-risk patients through clinical and echocardiographic markers may enhance prognosis and inform therapeutic strategies.

Mots-clés : Insuffisance cardiaque aiguë, dysfonctionnement ventriculaire droit, choc cardiogénique, facteurs prédictifs, mortalité hospitalière
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Introduction

Heart failure is a complex syndrome and a major cause of hospitalization and mortality worldwide. It is also associated with reduced physical function and often compromises quality of life, in addition to generating considerable costs. More than 64 million people worldwide are affected (1). Acute heart failure (AHF) is a syndrome characterized by the sudden onset (de novo heart failure) or deterioration (acutely decompensated heart failure, ADHF) of heart failure symptoms and signs, primarily linked to systemic congestion (2). Identifying factors associated with poor outcomes is critical for improving prognostication and patient management. The INTER-CHF (International Congestive Heart Failure) study provided epidemiological data on HF-associated mortality across continents. It revealed marked regional differences in mortality and associated factors, even after multivariate adjustment (3). Several sociodemographic, clinical, biochemical, and echocardiographic parameters have been implicated in predicting mortality in AHF, including advanced age (4), comorbidities such as hypertension, obesity, diabetes (5), impaired renal function (6), and biomarkers like NT-proBNP (7). Right ventricular dysfunction (8) and cardiogenic shock (9) have also emerged as key determinants of poor prognosis in AHF patients. However, the relative importance of these factors remains unclear. Hence, studies examining a broad range of variables in real-world clinical practice are needed to refine risk stratification tools and inform treatment decisions. We assumed that mortality among AHF patients is influenced by their medical history, comorbidities, as well as certain clinical and paraclinical characteristics. Based on this assumption, we conducted an analysis of relevant patients' data. Specifically, we examined sociodemographic, clinical, biological, echocardiographic and therapeutic characteristics to identify independent mortality predictors. This knowledge is essential for clinicians to better identify high-risk patients and optimize therapeutic interventions, potentially improving outcomes for AHF patients in acute care settings.

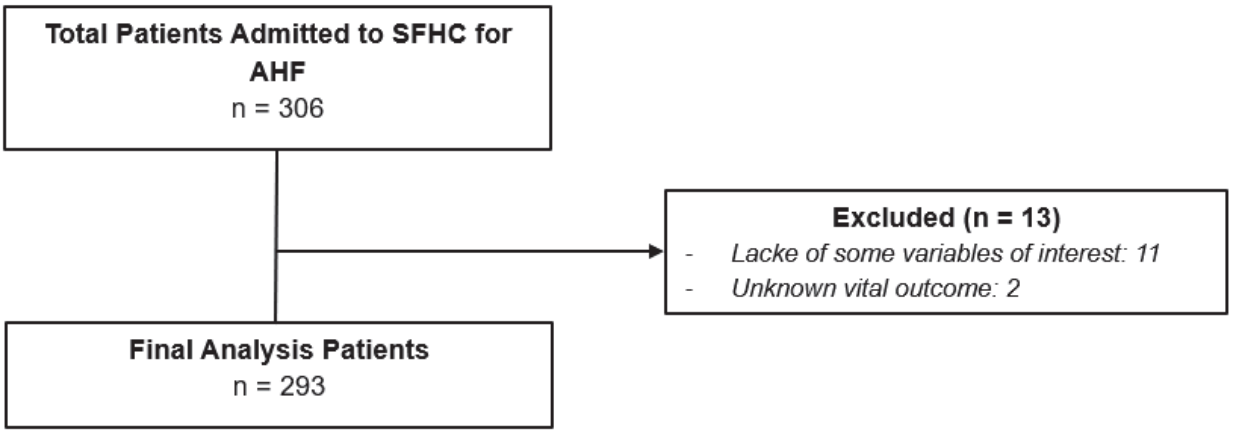
Methods

Study design and setting

This retrospective single-center analysis examined the records of patients with AHF who were admitted to the Cardiology Intensive Care Unit (CICU) at the Centre Hospitalier Sud Francilien (CHSF), in France.

Patient selection
This study included all men and women aged at least 18 years who had been hospitalized for AHF between January 1 and Jun 31, 2022.
Patients admitted for AHF whose medical records lacked variables of interest were excluded from the study.
Study procedures
All medical records of the patients admitted for AHF were retrieved and carefully reviewed by two researchers to obtain relevant data on the parameters of interest. These parameters included sociodemographic data (i.e., age, sex, marital status and ethnicity); cardiovascular risk factors (CVRFs) (i.e., hypertension, diabetes mellitus, dyslipidemia, cigarette smoking, obesity, and coronary heredity), medical history (i.e., ischemic heart disease, heart rhythm disease, known heart disease, chronic kidney failure, pulmonary embolism, hypothyroidism/hyperthyroidism, martial deficiency, chronic obstructive lung disease, sleep apnea syndrome, neoplasia, cardiac amyloidosis, dilated cardiomyopathy, chronic pulmonary heart, valvular heart disease, Takotsubo, hypertensive heart disease), clinical data (i.e., blood pressure, heart rate, oxygen saturation), the trigger factor of acute heart failure (acute coronary syndrome, Infection, anemia, severe hypertension, rapid atrial fibrillation, poor compliance, ventricular tachycardia), biological and echocardiographic characteristics, therapeutic profile, and vital outcome. laboratory results, medications, discharge status, and length of stay).
As this study was retrospective and based on electronic medical records, specific details regarding the assay methodology and laboratory equipment used were not available. All data were extracted as documented in the hospital information system.

Figure 1 summarizes the selection procedure.



SFHC = Sud Francilien Hospital Center, AHF = acute heart failure
Fig 1. Study flow chart

Operational definitions
The following definitions were used in this study:
A standardized diagnosis of AHF was established using the Framingham criteria and the guidelines of the European Society of Cardiology on the diagnosis and treatment of AHF (10). Both de novo presentation of AHF and acute presentation of typically decompensated HF were included.
Cardiogenic shock was diagnosed when AHF was accompanied by low systolic blood pressure (SBP <90 mmHg) for at least 30 minutes, or if support is needed to maintain SBP ≤ 90 mm Hg and oliguria (<0.5 mL/kg/h for minimum of 6 hours), or low cardiac index (<2.2 L/min/m^2) (11).
Right ventricular dysfunction (RVD) was defined as a TAPSE <16 mm, RV index of myocardial performance >0.40, and S′ <10 cm/s (12).
Chronic kidney disease (CKD) was defined as eGFR <60 ml/min per 1.73 m^2 and/or albumin-to-creatinine ratio ≥30 mg/g (13). Serum creatinine was used as the marker for eGFR, calculated using the CKD-EPI equation.
Obesity was defined as a BMI greater than or equal to 28 kg/m^2. 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.
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 (15). 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) (15). It was directly dosed using the dextran sulfate filtration technique if the triglyceride level was > 3.4 g/L (15). cigarette smoking was defined as use of any type of smoked tobacco product on a daily or occasional basis (16)

Left ventricular ejection fraction (LVEF) values were categorized into three groups according to the 2022 AHA/ACC/HFSA guideline for the management of heart failure (17), as follows: reduced (≤40%), mildly reduced (41–49%), and preserved (≥50%).

Statistical analysis

Data was compiled into an Excel 2010 database of cardiac insufficiency patient monitoring. After cleaning the database, the data was exported to IBM SPSS for Windows version 25 (IBM Corp., Armonk, NY) software for analysis. The results were presented in the form of means (standard deviation), medians (IQR) and proportions (%). Student's t tests were used to compare averages of continuous variables with a Gaussian distribution. The Mann-Whitney U test was used to compare medians, and either Pearson's chi square test or the exact Fischer test was performed to compare proportions in both groups. The normal distribution of each variable was evaluated using the Kolmogorov-Smirnov test. For the survival study, the Kaplan-Meier survival function was used to estimate the survival of patients. The comparison of Kaplan-Meier curves utilized the Log-rank test. Cox proportional risk regression was employed to identify predictors of mortality. The calculated risk ratio (HR) and their 95% confidence intervals (CI) allowed for estimating the degree of risk between mortality and independent variables. For all tests used, the statistical significance threshold was set at $p < 0.05$. Variables for multivariable Cox regression were selected based on both clinical relevance and statistical significance from the bivariate analysis.

Ethics approval

All experiments were performed in accordance with relevant guideline and regulations of Declaration of Helsinki. Data was fully anonymized before being accessed and the source of data was made from 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 306 patients admitted to the SFHC during the study period, thirteen patients were excluded: two due to unknown vital outcomes, and eleven due to missing biological data in their medical files. A total of 293 patients were selected for the final analysis.

General characteristics of the study population

The study population consisted of 293 patients hospitalized for acute heart failure during the study period, of which 189 (64.5%) were men and 104 (35.5%) women, with a sex ratio of 1.8 (in favor of men).

Sociodemographic, anthropometric and clinical characteristics at the study population entry based on vital outcome

Table 1 shows the sociodemographic, anthropometric and clinical characteristics of the study population according to the vital outcome. The average age of the patients was 72.4 ± 12.5 years (ranging from 28 to 98 years), with a majority falling under the age of 75. Most of the patients were male (64.5%), 50.5% were married and 79.2% were of Caucasian descent. The deceased patients were notably older than the survivors (Mean age: 77.2 ±10.5 years vs 71.8 ±12.7 years, p = 0.025), while other sociodemographic variables showed no significant differences between the two groups. The average BMI of the study population was 27.8 kg/m^2, with no statistically significant difference between survivors and the deceased.

In terms of vital signs, the systolic blood pressure was significantly lower (117.6 ±36.8 vs 130.1 ±29.5, p=0.033) on average in deceased patients compared to survivors. Compared to survivors, deceased group had significantly higher proportion of patients in cardiogenic shock compared to survivors (19.4% vs 2.7%, p <0.001), while the distribution of other types of acute heart failure was similar in both groups.

Table 1. Sociodemographic, anthropometric and clinical characteristics at the study population by vital outcome

Variables	Total N = 293 (%)	Survivors N = 262 (%)	Deceased N = 31 (%)	P value
Age (years)	72.4 ±12.6	71.8 ±12.7	77.2 ±10.5	**0.025**
Age groupe				0.141
< 75 years	154 (52.6)	141 (53.8)	13 (41.9)	
≥ 75 years	139 (47.4)	121 (46.2)	18 (58.1)	
Sex				0.842
Female	104 (35.5)	94 (35.9)	10 (32.3)	
Male	189 (64.5)	168 (64.1)	21 (67.7)	
Marital status				0.201
Unmarried	104 (35.5)	92 (35.1)	12 (38.7)	
Divorced	16 (5.5)	12 (4.6)	4 (12.9)	
Married	148 (50.5)	136 (51.9)	12 (38.7)	
Widower	25 (8.5)	22 (8.4)	3 (9.7)	
Ethnicity				0.374
Caucasian	232 (79.2)	205 (78.2)	27 (87.1)	
Maghrebian	31 (10.6)	28 (10.7)	3 (9.7)	
Black	30 (10.2)	29 (11.1)	1 (3.2)	
Weight (Kg)	74.2 ±17.9	73.7 ±18.0	79.4±17.3	0.397
BMI (Kg/m^2)	27.8 ±6.4	27.8 ±6.1	28.4 ±8.4	0.719
SBP (mmHg)	128.8 ±30.5	130.1 ±29.5	117.6 ±36.8	**0.033**
DBP (mmHg)	76.9 ±19.4	77.7 ±19.3	70.5 ±19.0	0.055
RR (Cpm)	30.2 ±5.7	30.2 ±5.8	30.8 ±5.0	0.586
SaO2 (°C)	90.4±7.3	90.4 ±7.4	90.6 ±6.5	0.834
Clinical type of HF				
Decompensated heart failure	173 (59)	155 (59.2)	18 (58.1)	1
APE	75 (25.6)	71 (27.1)	4 (12.9)	0.132
Isolated right heart failure	8 (2.7)	6 (2.3)	2 (6.5)	0.446
Cardiogenique Shock	13 (4.4)	7 (2.7)	6 (19.4)	**<0.001**
ACS + LV failure	24 (8.2)	23 (8.8)	1 (3.2)	0.472

Data are expressed as mean ± standard deviation, absolute (n) and relative (in percent) frequencies. BMI: Body mass index; SBP: systolic blood pressure; DBP: Diastolic blood pressure; RR: respiratory rate; APE = acute pulmonary edema; ACS + LV failure: acute coronary syndrome with left ventricular failure;

Cardiovascular risk factors, comorbidities and triggers of heart failure of patients according to vital outcome

Table 2 illustrates the cardiovascular risk factors and comorbidities of the study population based on the vital outcome. The table shows that the most common CVRF were arterial hypertension (63.8%), obesity (44.7%), smoking (43%), dyslipidemia (38.2%), and diabetes mellitus (37.2%). Survivors were more frequently hypertensive, compared to deceased patients (66 % vs 45.2 %, p = 0.037), with no statistically significant difference noted for other cardiovascular risk factors and comorbidities.

The table also indicates that the most frequently associated comorbidities with heart failure are atrial fibrillation (AF) (49.1%), iron deficiency (42.7%), chronic kidney disease (CKD) (27%), neoplasia (16.7), and sleep apnea syndrome (16.4%). Deceased patients had a higher frequency of AF compared to survivors (67.7 % vs 46.9 %, p = 0.045), while other comorbidities were present in similar proportions in both groups. The main triggering factors of acute heart failure attacks were ischemic attack (27%), anemia (17.4%), and infections (14.7%). In 26.3% of cases no triggering factor was identified. All triggering factors were present in statistically similar proportions between the living and deceased groups.

Table 2. Cardiovascular risk factors, comorbidities and triggers of heart failure of patients according to vital outcome

Variables	Total n = 293	Survivors n = 262	Deceased n = 31	p value
Hypertension	187 (63.8)	173 (66)	14 (45.2)	**0.037**
Diabetes	109 (37.2)	99 (37.8)	10 (32.3)	0.685
Obesity	131 (44.7)	121 (46.2)	10 (32.3)	0.199
Cigarette smoking	126 (43)	111 (42.4)	15 (48.4)	0.654
Coronary heredity	12 (4.1)	10 (3.8)	2 (6.5)	0.825
Dyslipidemia	112 (38.2)	103 (39.3)	9 (29)	0.358
Comorbidities				
Atrial Fibrillation	144 (49.1)	123 (46.9)	21 (67.7)	**0.045**
Hypothyroidism	40 (13.7)	38 (14.5)	2 (6.5)	0.338
Iron deficiency	125 (42.7)	108 (41.2)	17 (54.8)	0.689
Neoplasia	49 (16.7)	42 (16)	7 (22.6)	0.503
Chronic Kidney Disease	79 (27)	66 (25.2)	13 (41.9)	0.076
Heart disease	175 (59.7)	152 (58)	23 (74.2)	0.123
Ischemic Heart Cardiopathy	146 (49.8)	131 (50)	15 (48.4)	1
Cardiac amyloidosis	8 (2.7)	8 (3.1)	0 (0)	0.686
Dilated cardiomyopathy	51 (17.4)	49 (18.7)	2 (6.5)	0.147
Rhythmic heart disease	37 (12.6)	30 (11.5)	7 (22.6)	0.139
Valvular heart disease	25 (8.5)	20 (7.6)	5 (16.1)	0.207
Takotsubo cardiomyopathy	6 (2)	6 (2.3)	0 (0)	0.857
Hypertensive heart disease	11 (3.8)	10 (3.8)	1 (3.2)	1
Triggering factor				
ACS	79 (27)	69 (26.3)	10 (32.3)	0.625
Infection	43 (14.7)	35 (13.4)	8 (25.8)	0.113
None	77 (26.3)	72 (27.5)	5 (16.1)	0.253
Anemia	51 (17.4)	45 (17.2)	6 (19.4)	0.958
Severe hypertension	19 (6.5)	18 (6.9)	1 (3.2)	0.694
Rapid atrial fibrillation	8 (2.7)	8 (3.1)	0 (0)	0.686
Poor adherence	16 (5.5)	15 (5.7)	1 (3.2)	0.872
Ventricular Tachycardia	9 (3.1)	8 (3.1)	1 (3.2)	1

Data are expressed as absolute (n) and relative (in percent) frequencies. ACS: Acute coronary syndrome

Biological, echocardiographic and acute heart failure types of patients according to vital outcome

The biological and echocardiographic characteristics of the study population based on the vital outcome are presented in Table 3.

The table indicates that deceased patients had a significantly higher NT-proBNP level (17682.2±22139.2 pg/ml vs 8797 ± 10066.5, p = 0.038), as well as a lower glomerular filtration rate (50.6 ±28.1 ml/min/1.72m^2 vs 63.7 ± 33.4, p = 0.037), hemoglobin level (11.2±2.2 g/dl vs 12.7 ± 2.4, p = <0.001), natremia (135.9±4.4 mmol/l vs 137.7 ± 4.5, p =0.035) and LDL-C level (0.7±0.5 g/l vs 1.0 ±0.4, p = 0.029) compared to survivors. Deceased patients also exhibited right ventricular dysfunction more frequently (48.4% vs 21%, p <0.001). The different types of heart failure based on the left ventricular ejection fraction (Heart Failure with Reduced Ejection Fraction (HFrEF), Heart Failure with Preserved Ejection Fraction (HFpEF), and Heart Failure with Mid-Range Ejection Fraction (HFmrEF) were distributed similarly in both groups. Furthermore, table 3 shows that decompensated chronic heart failure was the most common type of acute heart failure (59%), followed by acute pulmonary edema (25.6%) and cardiogenic shock (4.4%).

Table 3. Biological, echocardiographic and acute heart failure types of patients according to vital outcome

Variables	Total n = 293	Survivors n = 262	Deceased n = 31	p value
NTproBNP (pg/ml)	9725.7±12158.1	8797 ± 10066.5	17682.2±22139.2	**0.038**
Troponine (pg/ml)	683.0 ± 2071.0	621.4 ± 1839.8	1176.5 ±3405.2	0.16
GFR (ml/min/1.72m^2)	62.3 ± 33.1	63.7 ± 33.4	50.6 ±28.1	**0.037**
Natremia (mmol/l)	137.5 ±4.5	137.7 ± 4.5	135.9±4.4	**0.035**
Kaliemia (mmol/l)	4.1 ± 0.6	4.1 ± 0.6	4.2±0.8	0.807
Glycemia(mmol/l)	1.4 ± 0.5	1.4 ± 0.5	1.6±0.5	0.159
Hemoblobin(g/dl)	12.5 ± 2.4	12.7 ± 2.4	11.2±2.2	**<.001**
Ferritine(µg/l)	334.0 ± 327.5	337.5 ± 328.1	309.5±328.8	0.696
CRP (mg/l)	41.8 ± 63.6	40.6 ± 63.6	52.7±63.6	0.347
LDL-c(g/l)	0.9 ± 0.5	1.0 ±0.4	0.7±0.5	**0.029**
HDL-c(g/l)	0.4 ± 0.1	0.4 ± 0.2	0.4±0.1	0.322
Triglycerides (g/l)	1.2 ± 0.6	1.2 ± 0.6	1.1±0.4	0.217
AIP	0.3 ± 1.1	0.4 ± 1.1	0.0 ± 1.0	0.13
CRI_II	2.4 ±1.3	2.4 ± 1.4	2.0 ± 1.2	0.129
CRI_I	3.3 ± 2.1	3.3 ± 2.2	3.0 ± 1.5	0.466
AC	2.3 ± 2.1	2.3 ± 2.2	2.0 ± 1.5	0.466
NHC	0.8 ± 0.6	0.8 ± 0.6	0.7 ± 0.4	0.372
Left ventricular volume(ml/m^2)	85.5 ± 37.8	84.5 ± 38.1	94.4 ± 34.2	0.215
LVEF (%)	39.0 ± 13.6	39.3 ± 13.5	36.6 ± 13.9	0.296
GLS (%)	9.4 ± 4.4	9.6 ± 4.3	7.0 ± 5.4	0.257
HF type according to LVEF				0.324

HFmEF	42 (14.3)	35 (13.4)	7 (22.6)	
HFpEF	74 (25.3)	68 (26)	6 (19.4)	
HFrEF	173 (59)	156 (59.5)	17 (54.8)	
Right Ventricular Dysfunction	70 (23.9)	55 (21)	15 (48.4)	**<0.001**

Data are expressed as mean±standard deviation, absolute (n) and relative (in percent) frequencies. NT-proBNP: N-Terminal Pro-B-Type Natriuretic Peptide; GFR : glomerular filtration rate; CRP = C-reactive protein; LDL-C: Low-density lipoprotein; HDL-C : High-density lipoprotein; AIP= atherogenic index of plasma, CRI_II = Castelli Risk Index II , CRI_I = Castelli Risk Index I, AC =Atherogenic coefficient; NHC: non-HDL-Cholesterol; LVEF : left ventricular ejection fraction; GLS = global longitudinal strain; HFmEF : Heart failure with mildly reduced ejection fraction; HFpFE: heart failure with preserved ejection fraction; HFrEF : heart failure with reduced ejection fraction

Acute phase treatment profile of study patients according to vital outcome

The acute phase treatment profile of the study patients according to the vital outcome is shown in Table 4. The table indicates that, in the acute phase, the most common treatments were diuretics (98.3%), oxygen therapy (65.2%), and angioplasty (25.6%). Only 16 (5.5%) patients received vasoactive amines. Deceased patients were more likely to have received vasoactive amines compared to survivors (22.6 % vs 3.4 %, p <0.001), while other treatments were administered in similar proportions in both groups.

Table 4. Acute phase treatment profile of study patients according to vital outcome

Variables	Total n = 293	Survivors n = 262	Deceased n = 31	P value
Diuretics	288 (98.3)	258 (98.5)	30 (96.8)	0.734
Oxygen	191 (65.2)	170 (64.9)	21 (67.7)	0.951
NIV	50 (17.1)	45 (17.2)	5 (16.1)	1
Vasoactive amines	16 (5.5)	9 (3.4)	7 (22.6)	<0.001
Risordan	36 (12.3)	33 (12.6)	3 (9.7)	0.847
Angioplasty	75 (25.6)	66 (25.2)	9 (29)	0.825

Data are expressed as absolute (n) and relative (in percent) frequencies. NIV = Non-invasive ventilation

Survival analyses and Predictors of in-hospital mortality in multivariate analysis

Patient survival analysis

Overall survival of AHF patients

The median time between admission and the end of patient hospitalization was 8.0 (EIQR:6.0-13.0) days with extremes ranging from 1 to 35 days. The cumulative survival rates of patients were 99.3% on day 2, 94.5% on day 7, 91.7% on day 14, and 90.3% on day 21, with this survival rate remaining constant until day 35.

Specific survival of AHF patients

Fugue 2 illustrates the specific survival of AHF patients. The survival rate of patients with AF was 86.7%, while patients without AF had a survival rate of 93.3%. Comparing the Kaplan-Meier curves of patients with AF revealed that survival was significantly higher (Log-rank, p=0.011) in patients without AF. The Kaplan-Meier curve for patients based on cancer status indicated that survival was significantly longer (Log-rank, p = 0.006) in patients without cancer (91%) compared to those with cancer (85.7%). The Kaplan-Meier curve comparing patients with and without CKD showed that survival was significantly higher in patients without CKD (92.5%) compared to those with CKD (83.5%)

(Log-rank, p = 0.042). Survival as a function of cardiogenic shock is depicted in the following figure. It is worth noting that survival was higher in patients without cardiogenic shock (91.8%) compared to those with cardiogenic shock (53.8%). This difference was found to be statistically significant (Log-rank, p < 0.001).

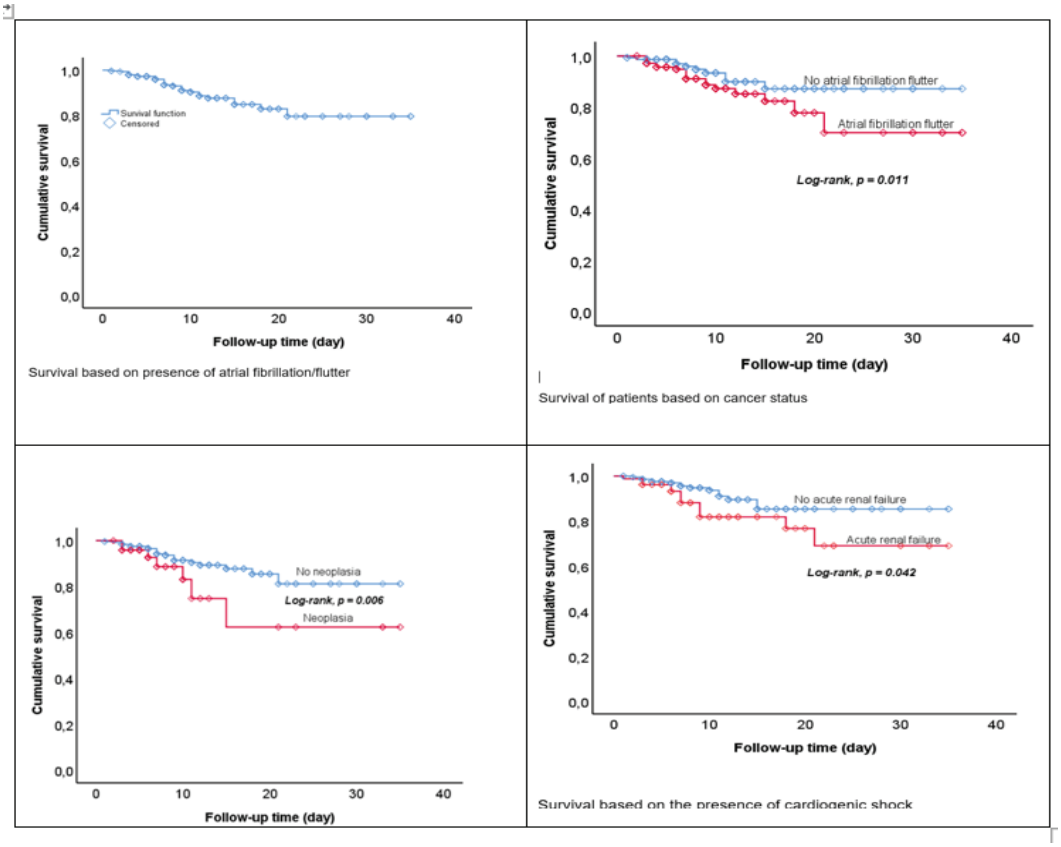


Figure 2. AHF patients' survival

Binary and multivariate Cox proportional hazard analysis to identify factors associated with in-hospital mortality among acute heart failure patients at CHSF

As shown in table 5, eleven variables had a p-value of less than 0.05 in the bivariate analysis. Therefore, these variables were included in the multivariate Cox proportional hazards models. However, only hypertension, cancer, CKD, anemia, NT-proBNP ≥ 10000 pg/ml, RV dysfunction, and cardiogenic shock were found to be significantly associated with in hospital mortality in the multivariate Cox regression.

Hypertension patients were twice as likely to be associated with in-hospital death compared to those without hypertension (adjusted hazard ratio (AHR) = 2.39, CI = 1.87-6.56, p = 0.011).

Furthermore, the following comorbidities were independently associated with the risk of in-hospital death: cancer, CKD, and anemia. In the presence of these comorbidities, the risk of in-hospital death was multiplied by two (AHR = 2.10, CI = 1.70-6.27, p=0.018), by three (AHR=2.64, CI=1.62-4.36, p=0.032) and by three (AHR=2.59, CI=1.67-4.01, p=0.017), respectively.

Moreover, the risk of in-hospital death was tripled in patients with NT-proBNP level of 10,000 pg/ml (AHR = 3.00, CI = 1.95-5.36, p = 0.005), almost quadrupled in those with RV dysfunction (AHR = 3.52, CI = 1.24-9.95, p = 0.018), and almost quintupled in those who experienced a cardiogenic shock (AHR = 4.74, CI = 2.93-14.1, p = 0.009).

Table 5. Binary and multivariate Cox proportional hazard analysis to identify factors associated with in-hospital mortality among acute heart failure patients at CHSF

Variables	Univariate analysis		Multivariate analysis	
	p-value	HR (95% CI)	p-value	aHR (95% CI)
Hypertension				
No		1		1
Yes	**0.013**	2.59 (1.22-5.48)	**0.011**	2.39 (1.87-6.56)
Atrial fibrillation/flutter				
No		1		1
Yes	**0.012**	2.85 (1.85-4.02)	0.817	1.12 (0.42-2.98)
Cancer				
No		1		1
Yes	**0.007**	2.93 (1.93-5.19)	**0.018**	2.10 (1.70-6.27)
CKD				
No		1		1
Yes	**0.005**	2.76 (1.99-4.37)	**0.032**	2.64 (1.62-4.36)
LLE				
No		1		1
Yes	**0.044**	2.14 (1.02-4.50)	0.276	1.69 (0.65-4.41)
Infection				
No		1		1
Yes	**0.034**	2.56 (1.63-3.86)	0.446	1.68 (0.44-6.41)
Anemia				
No		1		1
Yes	**0.003**	2.99 (1.60-6.63)	**0.017**	2.59 (1.67-4.01)
NT-proBNP (pg/ml)				
<10000		1		1
≥10000	**0.006**	3.28 (1.92-5.48)	**0.005**	3.00 (1.95-5.36)
LVV				
<75 (mL)		1		1
≥75 (mL)	**0.007**	2.31(1.94-5.66)	0.580	1.34 (0.47-3.84)
RV dysfunction				
No		1		1
Yes	**0.002**	3.40 (1.54-7.51)	**0.018**	3.52 (1.24-9.95)
Cardiogenic shock				
No		1		1
Yes	**0.001**	5.37 (2.03-14.18)	**0.009**	4.74 (2.93-14.13)

HR = hazard ratio, AHR = adjusted hazard ratio, CKD = chronic kidney disease, LVV = left ventricular volume, + RV = right ventricular.

Discussion

The results of this retrospective analysis of patients hospitalized for AHF provide critical insights into the factors associated with intra-hospital mortality in this population. By focusing on sociodemographic, clinical, biological, echocardiographic, and therapeutic variables, the study highlights several key predictors of mortality, many of which corroborate existing literature, while others offer new perspectives on the condition's progression and management.

Sociodemographic and Clinical Characteristics

The study population was mainly composed of elderly individuals, with an average age of 72.4 years. This is in line with findings from several large-scale registries, such as ADHERE (18) and OPTIMIZE-HF (19) in the USA, the European Heart Failure Surveys (EHFS) I (20) and II (21) and the ESC-HF Pilot Registry (22) in Europe,

as well as the international ALARM-HF registry(23), showing that acute heart failure predominantly affects older adults (2). The significant age difference between deceased and surviving patients (with deceased patients being older) reinforces the established notion that advancing age is a strong predictor of worse outcomes in heart failure patients (4). This finding is in line with a large body of evidence suggesting that age is a major risk factor for increased morbidity and mortality in cardiovascular disease, likely due to the cumulative effect of age-related cardiovascular changes and comorbidities (4, 24).

While sex distribution in the cohort showed a higher prevalence of men, the sex ratio did not appear to significantly influence mortality outcomes. This is in contrast with some studies where male gender has been associated with higher mortality rates in heart failure patients (25). The lack of a clear gender-related mortality differential in this study could be due to the specific patient population or other unmeasured confounders.

Cardiovascular Risk Factors and Comorbidities

The presence of common cardiovascular risk factors such as smoking, arterial hypertension, obesity, and diabetes mellitus is consistent with the well-established relationship between these conditions and the development of heart failure. In a post-hoc analysis from the Jackson Heart Study, a large prospective community-based observational study, Kamimura et al. found that current smoking was associated with an increased risk of incident HF hospitalization (26). In an analysis carried out on a sample of patients from four cohort studies (the Framingham Heart, Framingham Offspring, Chicago Heart Association Detection Project in Industry, and ARIC (Atherosclerosis Risk In Communities)), Ahmad *et al.* found that obesity, diabetes mellitus and arterial hypertension were associated with the occurrence of heart failure (5). However, the study also revealed that survivors were more likely to have hypertension than deceased patients, a finding that may reflect differences in disease management or the association between better blood pressure control and improved survival rates. This finding recalls the reverse (counterintuitive) association of hypertension and Cardiovascular Death in the Hemodialysis Population (27).

Notably, the higher prevalence of AF in deceased patients is a critical observation. AF is a common comorbidity in heart failure and is known to complicate the disease course, possibly through worsening symptoms, promoting thromboembolic events, and increasing the risk of stroke (28). The association between AF and mortality in this cohort emphasizes the need for more aggressive management of this arrhythmia in heart failure patients, especially given its potential to precipitate adverse outcomes.

Interestingly, no significant differences in the frequency of other comorbidities, such as CKD, iron deficiency, or neoplasia, between the two groups were noted. This suggests that while these conditions may play a role in the development and progression of heart failure, their impact on mortality in this cohort may not be as pronounced as other factors such as age, right ventricular dysfunction, or cardiogenic shock.

Biological and Echocardiographic Characteristics

Biological markers, including NT-proBNP, glomerular filtration rate (GFR), and natremia, were significantly worse in deceased patients. The elevation of NT-proBNP is a well-established biomarker for heart failure severity and prognosis, and its higher levels in deceased patients reflect the severe nature of their condition (7). Similarly, the lower GFR and natremia in deceased patients align with previous studies (29, 30), suggesting that renal dysfunction and electrolyte imbalances, often seen in heart failure, are significant contributors to poor outcomes. The relationship between heart failure and renal dysfunction (6) (also known as cardiorenal syndrome) is complex and bidirectional, and renal impairment is widely acknowledged as an independent predictor of mortality in heart failure.

The finding of right ventricular dysfunction being more prevalent in deceased patients is also noteworthy. Right ventricular dysfunction, which is often associated with acute decompensated heart failure and cardiogenic shock, is a critical predictor of mortality (8).

This highlights the need for early recognition and management of right ventricular failure, which is often overlooked in heart failure management.

In terms of the classification of heart failure, the study found no significant differences in the distribution of left ventricular ejection fraction categories (HFrEF, HFpEF, and HFmrEF) between survivors and deceased patients. However, deceased patients were more likely to be in cardiogenic shock, which is a well-known acute manifestation associated with high mortality rates in heart failure (9).

Therapeutic Profile and Mortality Predictors

The therapeutic profile revealed that vasoactive amines were more frequently administered to deceased patients, which likely reflects the severity of their condition, as these agents are typically reserved for patients in more critical states (31). This finding aligns with the systematic review and meta-analysis of Wang *et al*. (32) , who depicted an association between dobutamine therapy and poorer outcomes in patients with acute decompensated HF. The increased use of vasoactive medications in deceased patients underscores the importance of early and aggressive hemodynamic support in managing acute heart failure patients, especially those progressing to shock.

Survival Analysis and Kaplan-Meier Estimates

The median hospital stay was 8 days, with survival dropping to 90.3% by day 21 and plateauing thereafter. Stratified survival analysis using Kaplan-Meier curves demonstrated significantly poorer outcomes in patients with AF (86.7% vs 93.3%, p = 0.011), neoplasia (85.7% vs 91%, p = 0.006), CKD (83.5% vs 92.5%, p = 0.042), and cardiogenic shock (53.8% vs 91.8%, p < 0.001). These results are consistent with previous reports from large international registries such as ADHERE (33) and ALARM-HF (23), which also identified AF and CKD as significant contributors to early mortality in hospitalized heart failure patients (23, 33). Additionally, the impact of cardiogenic shock on mortality, as indicated by a sharp drop in survival to 53.8%, supports findings from the ESC-HF Pilot study (34) and more recent analyses by Jung *et al.* (35), highlighting cardiogenic shock as one of the most powerful predictors of adverse in-hospital outcomes. The observed difference in survival rates among patients with cancer underscores growing concerns regarding the intersection of cardiology and oncology, as outlined by Bloom *et al.* (36), suggesting that oncologic comorbidities may worsen heart failure prognosis through inflammatory and iatrogenic mechanisms. These findings provide compelling evidence of the impact of comorbidities on short-term prognosis and suggest the need for aggressive monitoring and multidisciplinary management in these subgroups.

Predictors of Mortality

The multivariate Cox regression model identified seven independent predictors of in-hospital mortality: hypertension, cancer, chronic kidney disease (CKD), anemia, NT-proBNP ≥ 10,000 pg/ml, right ventricular (RV) dysfunction, and cardiogenic shock. The relative risks ranged from a doubling of risk (hypertension and cancer) to nearly a five-fold increase in risk (cardiogenic shock, aHR = 4.74, p = 0.009), emphasizing the complex interplay of systemic comorbidities and cardiac compromise in determining outcomes.

The identification of hypertension as a mortality predictor is particularly noteworthy. Although commonly associated with chronic heart failure, its presence in the acute setting may reflect longstanding vascular damage and altered hemodynamic response, potentially exacerbating decompensation. This association contrasts with earlier findings where chronic hypertension was considered protective; our results support the hypothesis that untreated or severe hypertension contributes to adverse outcomes in acute care settings.

Malignancy (aHR = 2.10, p = 0.018) also emerged as a significant risk factor. This finding is consistent with Manuel Méndez-Bailón et al's research, which showed that patients with HF and cancer have worse survival rates compared to HF patients without cancer (37). This finding suggest that cancer-related inflammation, treatment-related cardiotoxicity, or delayed diagnosis may worsen outcomes. Similarly, CKD (aHR = 2.64, p = 0.032) and anemia (AHR = 2.59, p = 0.017) are established contributors to cardiorenal syndrome and impaired oxygen

delivery, both of which critically compromise cardiac performance (38, 39). The prognostic significance of NT-proBNP ≥ 10,000 pg/ml (AHR = 3.00, p = 0.005) aligns with its established role as a biomarker for short-term prognosis (40) , cardiac wall stress, and neurohormonal activation (41). In this cohort, it proved to be a strong indicator of disease severity and a predictor of mortality. Right ventricular dysfunction (AHR = 3.52, p = 0.018) is increasingly recognized as an independent predictor of adverse outcomes (42) , reflecting the detrimental effects of biventricular failure, venous congestion, and systemic hypoperfusion. Our findings confirm the need for echocardiographic surveillance of RV function in all AHF patients. Cardiogenic shock was found to be the strongest independent predictor of mortality, nearly quintupling the risk of in-hospital death. The predictive value of cardiogenic shock for mortality in acute heart failure patients has been demonstrated in several studies (43-45). This highlights the urgent need for rapid identification and advanced circulatory support in patients presenting with or developing shock. The dramatic impact of cardiogenic shock underscores its role not only as a consequence of severe cardiac dysfunction but also as a therapeutic turning point requiring prompt escalation of care (46, 47). Together, these findings underscore the multifactorial nature of AHF-related mortality and support a multidimensional approach to early risk stratification that includes clinical presentation, comorbidity burden, laboratory values, and echocardiographic findings.

Strengths and limitations of the study

Strengths of this study include retrospective design (providing valuable real-world data from a large sample of 293 patients, offering a solid foundation for identifying mortality predictors), comprehensive data (including a wide range of sociodemographic, clinical, biological, echocardiographic, and therapeutic variables, enhancing the robustness of the analysis), and multivariate analysis (identifies independent mortality predictors, adding strength to the conclusions regarding the factors contributing to poor outcomes). This study offers an important contribution to the understanding of mortality in AHF. In addition, it provides guidance for future research and clinical practices in managing this challenging and high-risk patient population. However, some limitations should be mentioned. As a retrospective study, it is subject to potential biases related to missing or incomplete data, limiting causal inferences. In addition, like most retrospective studies, we were unable to specify the assay methodology or laboratory platforms used because this information was not systematically documented in the patient records. Moreover, the findings may not be fully generalizable to other healthcare settings or populations, as the study was conducted at a single hospital. Furthermore, the study focuses on in-hospital mortality without assessing long-term outcomes, which would provide a more comprehensive understanding of patient prognosis.

Conclusion

The study shows that mortality in AHF is multifaceted, with substantial contributions from both cardiac and extracardiac causes. Timely detection of patients exhibiting elevated NT-proBNP levels, right ventricular failure, cardiogenic shock, and significant comorbidities such as chronic kidney disease, anemia, and neoplasia may provide more assertive and tailored therapies. These results highlight the importance of careful risk assessment and could direct the development of improved prognostic models for AHF. To improve survival outcomes in this at-risk population, more multicenter prospective studies are needed to validate these predictors and look into treatment options targeted at modifiable risk factors.

Conflict of interest

The authors declared that they have any conflict of interest.

Contribution for authors

FNN and BPK wrote the first draft of the manuscript; FNN and AMK prepared the database; ANN carried out the statistical analyses; FNN, JMM, YDM, CMK, GMI, YVM, AEAE, BMM, FPI, TKP, ESL, AMK, PG, FB, PMM, BB, TMT, and BPK have read and revised manuscript; BKP was the scientific coordinator of the work.

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