Low urinary sodium predicts short-term mortality in acute heart failure: Insights from a prospective study

Natriurèse basse : facteur prédicitif de mortaité à court terme dans l'insuffisance cardiaque aigue

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Summary

Introduction : Electrolyte disturbances reflect the complex interaction between renal dysfunction, neurohormonal activation, and congestion in acute heart failure (AHF). Urinary sodium (UNa) has emerged as a potential biomarker of diuretic response and decongestive effectiveness, but its prognostic value for mortality in AHF remains incompletely defined.

This study aimed to investigate the association between low UNa measured early during hospitalization and mortality in patients admitted for AHF.

Methods: This single-centre prospective study was conducted between February and December 2024 in the cardiology department of the Security Forces Hospital in La Marsa. Consecutive adult patients (≥18 years) admitted to the intensive care unit for de novo AHF or acute decompensation of chronic heart failure (CHF) were included. Patients receiving chronic haemodialysis or with severe baseline renal dysfunction were excluded. Clinical, biological, and echocardiographic data were collected during the index hospitalization. UNa was measured 24 hours after admission. Patients were followed to assess all-cause mortality, including in-hospital mortality and mortality at 3 and 6 months.

Results: The median age was 66 years [58–74]. Ischaemic heart disease was present in 46% of patients. The mean left ventricular ejection fraction (LVEF) was 41.4 ± 15.9%. During hospitalization, 62.1% of patients developed type 1 cardiorenal syndrome (CRS). The mean UNa concentration was 76.4 ± 32.0 mmol/L. In multivariable analysis, low UNa was independently associated with increased mortality (OR 5.62, 95% CI 1.68–18.81; p = 0.005), together with higher serum creatinine at 48 hours and impaired right ventricular function assessed by TAPSE. Receiver operating characteristic (ROC) analysis demonstrated good discriminatory performance of UNa for predicting mortality (AUC = 0.82). The cut-off value of UNa ≤46 mmol/L showed a negative predictive value of 92.8%.

Conclusion: Low UNa measured 24 hours after admission is independently associated with increased short-term mortality in patients with AHF. These findings highlight the potential value of UNa as a simple and readily available biomarker for risk stratification and assessment of decongestive response in AHF.

Mots-clés

Acute heart failure, Urinary sodium, Prognosis, All-cause mortality

Résumé

Introduction : Les troubles électrolytiques reflètent l'interaction complexe entre dysfonction rénale, activation neuro-hormonale et congestion dans l'insuffisance cardiaque aiguë (ICA). Le sodium urinaire (NaU) s'est récemment imposé comme un biomarqueur potentiel de la réponse aux diurétiques et de l'efficacité de la décongestion. Toutefois, sa valeur pronostique concernant la mortalité dans l'ICA reste insuffisamment définie. Cette étude avait pour objectif d'évaluer l'association entre un NaU bas mesuré précocement au cours de l'hospitalisation et la mortalité chez les patients admis pour ICA.

Méthodes: Il s'agit d'une étude prospective monocentrique menée entre février et décembre 2024 dans le service de cardiologie de l'Hôpital des Forces de Sécurité Intérieure de La Marsa. Les patients adultes consécutifs admis en unité de soins intensifs pour une ICA de novo ou une décompensation aiguë d'insuffisance cardiaque chronique ont été inclus. Les patients sous hémodialyse chronique ainsi que ceux présentant une insuffisance rénale sévère à l'admission ont été exclus. Le NaU a été mesuré 24 heures après l'admission. Le suivi a permis d'évaluer la mortalité hospitalière ainsi qu'à 3 et 6 mois.

Résultats: L'âge médian des patients était de 66 ans [58–74]. Une cardiopathie ischémique était retrouvée chez 46 % des patients. La fraction d'éjection ventriculaire gauche (FEVG) moyenne était de 41,4 ± 15,9 %. Au cours de l'hospitalisation, 62,1 % des patients ont développé un syndrome cardiorénal de type 1. La concentration moyenne de NaU était de 76,4 ± 32,0 mmol/L. En analyse multivariée, un NaU bas était indépendamment associé à une augmentation du risque de mortalité (OR 5,62 IC95 % 1,68–18,81 ; p=0,005), de même qu'une élévation de la créatininémie à 48 heures et une altération de la fonction ventriculaire droite évaluée par le TAPSE. L'analyse ROC a montré une bonne performance discriminante du NaU pour prédire la mortalité (AUC = 0,82). Le seuil de NaU ≤46 mmol/L présentait une valeur prédictive négative de 92,8 %.

Conclusion: Un NaU bas à 24 heures est associé de manière indépendante à la mortalité à court terme chez les patients hospitalisés pour ICA.

Keywords

Insuffisance cardiaque aiguë, Sodium urinaire, Pronostic, Mortalité globale

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INTRODUCTION

Heart failure (HF) represents a major public health challenge worldwide and is associated with substantial morbidity and mortality [1,2]. Its incidence increases with age, affecting nearly 20% of individuals older than 75 years, and it remains the leading cause of hospitalization among patients over 65 years in developed countries [3,4]. AHF accounts for a large proportion of these admissions and is associated with considerable clinical and economic burden [2,3,5]. The period following hospitalization for AHF is particularly critical, with high rates of mortality and rehospitalisation during the first year after discharge [4]. Data from the European Society of Cardiology (ESC) HF Long-Term Registry reported a 1-year all-cause mortality rate of 23.6% after hospitalization for AHF, with the combined incidence of death or HF rehospitalisation reaching 40.1% within the first year [6]. Similarly, the EVOLUTION HF study including 263,525 patients reported a 1-year mortality rate of 28.4 per 100 patient-years following discharge [7]. In Tunisia, the NATURE-HF registry also highlighted the prognostic burden of HF, reporting a 1-year mortality rate of 13% among HF patients overall and 22.8% among those hospitalized for AHF [8].

A key feature of HF is chronic sodium retention leading to extracellular volume expansion and congestion [9]. Although sodium homeostasis is normally maintained through tightly regulated renal excretion and interstitial buffering mechanisms [10], this balance is disrupted in HF due to neurohormonal activation and haemodynamic alterations that impair the renal natriuretic response [11]. Loop diuretics promoting natriuresis remain the cornerstone of AHF treatment, aiming to achieve effective decongestion, which has been associated with improved survival and fewer rehospitalisations [12–14]. However, assessment of decongestion remains challenging, and residual congestion at discharge is frequent and associated with worse outcomes [12]. In this context, urinary sodium (UNa) has emerged as a potential biomarker of diuretic response, with low UNa levels associated with poor decongestion and an increased risk of rehospitalisation or cardiovascular mortality [9,12]. Accordingly, the present study sought to evaluate the prognostic significance of early UNa excretion and its association with mortality in patients hospitalized for AHF.

METHODS

Study population

This single-centre prospective study was conducted between February and December 2024 in the cardiology department of the Security Forces Hospital in La Marsa. Consecutive adult patients (≥18 years) admitted to the intensive care unit for acute de novo HF or acute decompensation of CHF were considered for inclusion. Patients receiving chronic haemodialysis and those with severe baseline renal dysfunction defined as creatinine clearance <30 mL/min were excluded. Clinical, biological, and echocardiographic data were collected during the index hospitalization. UNa measurements were performed at 24 hours after admission. Patients were followed during hospitalization and after discharge to assess all-cause mortality, including in-hospital mortality as well as mortality at 3 and 6 months. Patients were excluded if they declined or withdrew informed consent or were lost to follow-up.

Data collection

During the index hospitalization, demographic, clinical, electrocardiographic, biological, and echocardiographic data were prospectively collected for all patients. Baseline characteristics included cardiovascular risk factors, history of chronic kidney disease (CKD), atrial fibrillation (AF), coronary artery disease (CAD), and underlying heart disease. Clinical evaluation included haemodynamic parameters, signs of left- and right-sided HF, precipitating factors for acute decompensation, and diuresis monitoring. Laboratory analyses included renal function parameters, cardiac biomarkers, electrolytes, inflammatory markers, liver function tests, and UNa concentration. A standard 12-lead electrocardiogram was performed in all patients. Transthoracic echocardiography was performed during hospitalization to assess left ventricular (LV) size and systolic function, right ventricular (RV) function, pulmonary artery systolic pressure (PASP), and the presence of significant valvular heart disease. Data on loop diuretic therapy, including cumulative dose and duration of treatment (in days), were collected, as well as the use of haemodynamic support and renal replacement therapy (RRT). Guideline-directed medical therapy (GDMT) was also recorded, including initiation or up-titration at hospital discharge when clinically appropriate.

Urinary sodium assessment

UNa concentration was measured within the first 24 hours after admission using a spot urine sample collected after initiation of intravenous diuretic therapy. Samples were analysed in the hospital's central laboratory using standard automated biochemical methods, and UNa levels were expressed in mmol/L. UNa concentration was used as a marker of early natriuretic response to diuretic treatment in patients with AHF. Low urinary sodium was defined according to the 2021 ESC HF guidelines as a urinary sodium concentration <50–70 mmol/L [15], reflecting an inadequate natriuretic response to diuretic therapy.

Analytical study

Categorical variables were presented as frequencies and percentages, whereas continuous variables were reported as mean ± standard deviation or median with interquartile range, depending on data distribution. Comparisons between groups were performed using the chi-square test or Fisher's exact test for categorical variables, and the Student's t-test or Mann–Whitney U test for continuous variables, as appropriate. Variables showing a p value <0.05 in univariable analyses were entered into multivariable logistic regression models to identify independent predictors of outcomes. A two-tailed p value <0.05 was considered statistically significant. All participants provided oral informed consent prior to inclusion, and confidentiality of patient data was maintained throughout the study.

RESULTS

Among 103 patients admitted with AHF, either de novo or due to acute decompensation, seven were not included according to predefined non-inclusion criteria. Nine additional patients were excluded because of loss to follow-up or missing urinary sodium measurement within the first 24 hours. The final study population therefore comprised 87 patients. The flowchart illustrating the patient selection process is presented in Figure 1.

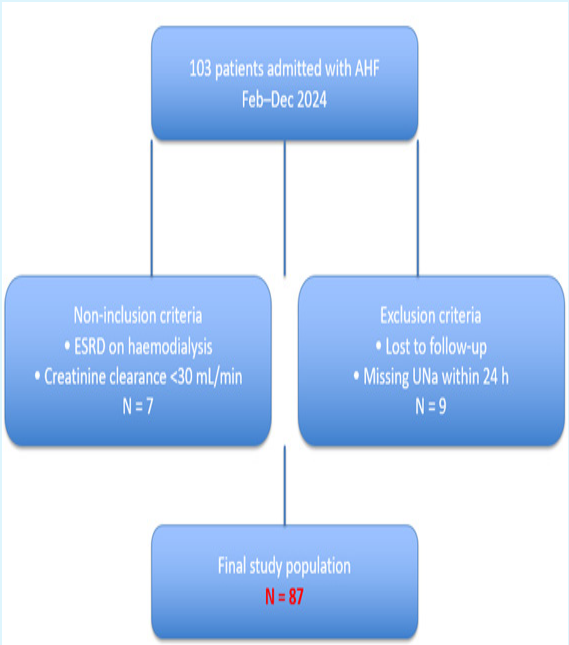

Figure 1. Flowchart of study population selection

AHF: Acute heart failure, ESRD: end-stage renal disease, UNa = urinary sodium

The baseline demographic, clinical, biological and echocardiographic characteristics of the study population are presented in Table 1. The median age of the cohort was 66 years [58–74], and the majority of patients were male (70.1%). Cardiovascular risk factors were highly prevalent, including hypertension (54.0%), diabetes mellitus (67.8%), dyslipidaemia (64.4%) and smoking (39.1%). Chronic kidney disease (CKD) was present in 63.2% of patients, while ischaemic heart disease and atrial fibrillation were reported in 46% and 55.2% of cases, respectively. During hospitalization, 62.1% of patients developed type 1 CRS. The mean heart rate and systolic blood pressure at admission were 102.7 ± 27.2 bpm and 121.3 ± 23.2 mmHg, respectively. The median NT-proBNP level was 4037 pg/mL [2125–6970], and the mean UNa concentration was 76.4 ± 32.0 mmol/L. The mean LV ejection fraction was 41.4 ± 15.9%, with 46% of patients presenting with HFrEF, 18% with HFmrEF and 36% with HFpEF. RV dysfunction was observed in 39.1% of patients, with a mean TAPSE/PASP ratio of 0.32 ± 0.14.

Table 1. Baseline demographic, clinical, biological, and echocardiographic characteristics of the study population

Variable	Value n, (%)
Age, years	66 [58–74]
Male sex, n (%)	61 (70.1)
BMI, kg/m²	26.0 [23.3–32.0]
Hypertension	47 (54.0)
Diabetes mellitus	59 (67.8)
Dyslipidaemia	56 (64.4)
Smoking	34 (39.1)
CKD	55 (63.2%)
Ischeamic heart disease	40 (46%)
AF	48 (55.2)
Infection	19 (21.8)
Myocardial ischaemia	18 (20.7)
CRS	54 (62.1%)
Heart rate, bpm	102.7 ± 27.2
Systolic blood pressure, mmHg	121.3 ± 23.2
Oxygen saturation, %	91.9 ± 3.9
Haemoglobin, g/dL	12.0 ± 2.14
NT-proBNP, pg/mL	4037 [2125–6970]
Creatinine, µmol/L	113.1 ± 44.3
UNa, mmol/L	76.4 ± 32.0
LVEF, %	41.4 ± 15.9
HFrEF, n (%)	40 (46)
HFmrEF, n (%)	16 (18)
HFpEF, n (%)	31 (36)
RV dysfunction, n (%)	34 (39.1)
PASP, mmHg	58.9 ± 17.6
TAPSE/PASP ratio	0.32 ± 0.14

BMI: Body mass index, CKD: Chronic kidney disease, AF: Atrial fibrillation, CRS: Cardio-renal syndrome, HF: Heart failure; HFrEF: Heart failure with reduced ejection fraction; HFmrEF: Heart failure with mildly reduced ejection fraction; HFpEF: Heart failure with preserved ejection fraction; LVEF: Left ventricular ejection fraction; NT-proBNP: N-terminal pro-B-type natriuretic peptide, RV: Right ventricular, PASP: Pulmonary artery systolic pressure; UNa: Urinary sodium.

During hospitalization, loop diuretics were mainly administered as intravenous bolus (58.6%), with continuous infusion or combined strategies used in 20.7% of cases each. Respiratory support was required in 28.7% of patients with nasal oxygen and 10.3% required non-invasive ventilation. Thiazide diuretics were added in 21.8% of cases. Patients with low UNa levels required a longer duration of intravenous loop diuretic therapy compared with those with higher UNa levels (Figure 2).

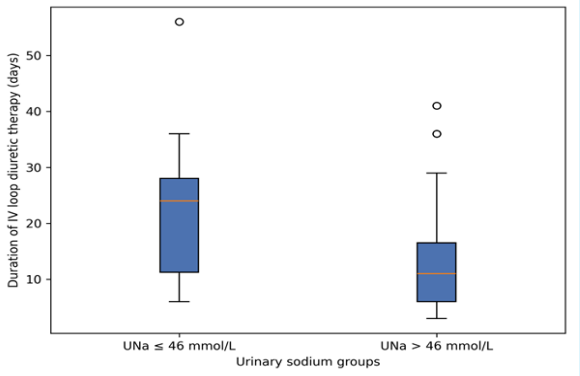

Figure 2. Duration of intravenous loop diuretic therapy according to UNa levels.

IV: Intravenous loop, UNa: Urinary sodium

GDMT was initiated or up-titrated during hospitalization, including beta-blockers (92.5%), angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) (56.3%), mineralocorticoid receptor antagonists (MRA) (28.8%), and sodium–glucose cotransporter 2 (SGLT2) inhibitors (68.8%). During follow-up, a total of 14 patients (16.1%) died. In-hospital mortality occurred in 7 patients (8.0%), while 2 deaths (2.3%) were observed at 3 months and 5 deaths (5.8%) at 6 months after discharge. Mortality outcomes are summarized in Table 2.

Table 2. All-cause mortality during hospitalization and follow-up

Outcome	n (%)
All-cause mortality	14 (16.1)
In-hospital mortality	7 (8.0)
3-month mortality	2 (2.3)
6-month mortality	5 (5.8)

ANALYTICAL ANALYSIS

Univariable analysis

Baseline demographic characteristics, cardiovascular risk factors, and clinical findings

Baseline demographic characteristics, cardiovascular risk factors, and clinical findings according to survival status are presented in Table III. Patients who died were older and more frequently had CKD and CRS. They presented with lower systolic and mean arterial blood pressure, lower oxygen saturation and markedly reduced urine output. Cardiac amyloidoisis was also more prevalent among non-survivors, whereas other baseline characteristics and HF phenotypes were comparable between groups.

Table 3. Baseline demographic, clinical, and cardiac Characteristics according to rehospitalisation status

Variable	Mortality (+) n=14	Mortality (-) n=73	p-Value
Age (Years)	70.00±12.10	64.20±13.00	0.041
Gender			
Men	12 (85.7%)	49 (67.1%)	0.214
Women	2 (14.3%)	24 (32.9%)	
Obesity	4 (28.6%)	27 (37.0%)	0.570
BMI	26.60±6.10	28.00±5.80	0.451
Hypertension	7 (50.0%)	40 (54.8%)	0.970
Diabetes	10 (71.4%)	49 (67.1%)	1.000
Dyslipidaemia	10 (71.4%)	46 (63.%)	0.762
Smoking	5 (35.7%)	29 (39.7%)	1.000
CAD	8 (57.1%)	38 (52.1%)	0.954
CKD	12 (85.7%)	43 (58.9%)	0.032
AHF de novo	7 (50.0%)	43 (58.9%)	0.747
AF	7 (50.0%)	41 (56.2%)	0.895
HF phenotypes			
HFpEF	6 (42.9%)	25 (34.3%)	0.544
HFmrEF	3 (21.4%)	13 (17.8%)	0.716
HFrEF	5 (35.7%)	35 (47.9%)	0.583
CRS	12 (85.7%)	42 (57.5%)	0.018
Ischaemic HD	5 (35.7%)	35 (47.9%)	0.570
Valvular HD	4 (28.6%)	12 (16.4%)	0.279
Rythmic HD	0 (0%)	10 (13.7%)	0.355
Idiopathic HD	1 (7.1%)	4 (5.5%)	0.202
Mixed HD	1 (7.1%)	5 (6.8%)	1.000
Inflammatory HD	0 (0%)	5 (6.8%)	0.588
Infiltrative HD Amyloidoisis	2 (14.3%)	3 (4.1%)	0.041
HR	103.10±24.80	102.70±27.80	0.956
SBP	113.9±25.20	122.70±22.70	0.041
DBP	66.90±11.30	70.30±14.00	0.326
MAP	80.50±14.70	86.90±17.20	0.032
SpO2	89.40±5.20	92.40±3.40	0.004
Left HF	1 (7.1%)	13 (17.8%)	0.451
Right HF	0 (4.5%)	2 (2.7%)	1.000
BiV HF	13 (92.9%)	58 (79.5%)	0.451
Hourly urine output (mL/H)	74.20±57.20	138.70±40.80	<0.001

BMI: Body mass index, CAD: Coronary artery disease, CKD: Chronic kidney disease, CRS: Cardio-renal syndrome, HD: Heart disease, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, SpO2: Peripheral capillary oxygen saturation, HF: Heart failure.

Electrocardiographic characteristics

No electrocardiographic parameter was significantly associated with mortality (Table 4).

Table 4. Electrocardiographic characteristics according to mortality status

Parameter	Mortality (+) n=14	Mortality (-) n=73	p-Value
SR	9 (64.3%)	35 (47.9%)	0.389
Paced rhythm	0 (0%)	3 (4.1%)	1.000
PR interval (ms)	142.90±97.50	88.50±95.00	0.071
QRS duration (ms)	114.60±26.50	101.9±23.8	0.080
LBBB	5 (35.7%)	12 (16.4%)	0.137
RBBB	3 (21.4%)	10 (13.7%)	0.432

SR: Sinus rhythm, LBBB: Left Bundle branch block, RBBB: Right bundle branch block

Biological characteristics

Biochemical characteristics according to mortality status are presented in Table 5. Patients who died had significantly higher NT-proBNP levels (5641 [4100–10520] vs 3415 [1900–6225] pg/mL, p=0.023), lower haemoglobin levels (10.76±1.37 vs 12.24±2.18 g/dL, p=0.003), and worse renal function at admission, reflected by higher urea and serum creatinine levels. Renal impairment remained more pronounced at 48 hours among non-survivors, with significantly higher creatinine levels and lower creatinine clearance. Urinary sodium levels were markedly lower in patients who died (45.6±26.9 vs 82.3±29.6 mmol/L, p<0.001). In addition, elevated serum lactate (≥2 mmol/L) was significantly more frequent among non-survivors.

Table 5. Biochemical characteristics according to mortality status

Parameter	Mortality (+) n=14	Mortality (-) n=73	p-Value
NT-ProBNP (pg/mL)	5641 [4100-10520]	3415 [1900-6225]	0.023
Hs-Tn (ng/L)	54.5 [26-412]	28 [14-120]	0.335
CRP (mg/L)	54 [11.5-234.5]	29 [12-68]	0.210
HgB (g/dl)	10.76±1.37	12.24±2.18	0.003
Urea T0 (mmol/L)	15.06±8.99	9.60±4.30	0.043
sCr T0 (umol/l)	142.64±57.68	107.37±39.24	0.044
ClCr T0 (mL/min)	59.57±43.01	68.45±29.74	0.471
Urea H48 (mmol/l)	19.46±11.19	14.07±22.70	0.186
sCr H48 (umol/L)	237.07±139.98	136.47±60.77	0.019
ClCr H48 (mL/min)	35.93±20.92	55.66±27.52	0.006
Na+(mmol/L)	131.07±6.84	134.48±6.51	0.103
K+ (mmol/l)	4.28±.055	3.98±6.53	0.077
Cl- (mmol/L)	95.50±7.58	97.90±6.53	0.283
UNa (mmol/L)	45.57±26.94	82.29±29.57	<0.001
Serum lactate≥2 mmol/L	8 (57.1%)	2 (2.7%)	<0.001

BMI: Body mass index, CAD: Coronary artery disease, CKD: Chronic kidney disease, CRS: Cardio-renal syndrome, HD: Heart disease, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, SpO2: Peripheral capillary oxygen saturation, HF: Heart failure.

Echocardiographic characteristics

Left ventricular characteristics

LV structure, systolic and diastolic function, and valvular heart disease severity were similar between survivors and non-survivors, with only a non-significant trend toward higher pulmonary congestion as reflected by B-lines (Table 6).

Table 6. Baseline demographic, clinical, and cardiac Characteristics according to rehospitalisation status

Parameter	Mortality (+) n=14	Mortality (-) n=73	p-Value
LVEF (%)	42.00 [26.00–52.00]	47.00 [28.00–54.25]	0.552
GLS (%)	−11.80±5.07	−12.08±4.27	0.839
LVEDD (mm)	58.30±10.60	56.57±9.25	0.539
LVESD (mm)	44.23±12.15	40.93±13.26	0.399
LVEDV (mL)	142.00 [103.00–171.00]	131.00 [117.00–167.00]	0.933
LVESV (mL)	75.00 [42.00–123.00]	74.00 [45.00–105.00]	0.722
LVMi (g/m²)	120.00 [82.75–148.50]	113.00 [85.00–136.00]	0.615
LAVi (mL/m²)	57.50 [44.25–74.00]	57.00 [47.00–70.00]	0.725
E/e'	14.00 [10.00–18.00]	13.00 [10.25–16.75]	0.763
LVOT VTI (cm)	16.31±5.60	16.92±5.13	0.720
CO (L/min)	4.10±0.94	4.29±1.27	0.545
CI (L/min/m²)	2.20 [1.70-2.60]	2.30 [1.85-2.60]	0.567
B lines	13 (92.9%)	48 (65.8%)	0.056
Pleural effusion	8 (57.1%)	35 (47.9%)	0.572
Severe MS	1/14 (7.1%)	2/73 (2.7%)	0.413
Severe MR	2/14 (14.3%)	5/73 (6.8%)	0.313
Severe AS	2/14 (14.3%)	2/73 (2.7%)	0.120
Severe AR	0/14 (0.0%)	2/73 (2.7%)	1.000

LVEF: Left ventricular ejection fraction, GLS: Global longitudinal strain, LVEDD : Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, LVEDV: Left ventricular end-diastolic volume, LVESV: Left ventricular end-systolic volume, LVMi: Left ventricular mass index, LAVi: Left atrial volume index, E/e': Ratio of mitral inflow E-wave to mitral annular e' wave, LVOT VTI: Right ventricular outflow tract velocity time integral, CO: cardiac output, CI: Cardiac index, MS: Mitral stenosis, MR: Mitral regurgitation, AS: Aortic stenosis, AR: Aortic regurgitation

Right ventricular characteristics

Echocardiographic parameters according to mortality status are summarized in Table 7. Most RV dimensions and functional indices were comparable between groups. However, non-survivors had significantly lower TAPSE values (15.79±3.24 vs 18.16±3.86 mm, p=0.024), higher right atrial pressure (RAP) (15.0 [13.75–20.0] vs 10.0 [5.0–15.0] mmHg, p=0.027), and a higher prevalence of non-compliant inferior vena cava (IVC) (92.9% vs 63.0%, p=0.031). Other parameters, including PASP and the TAPSE/PASP ratio, did not differ significantly between groups.

Table 7. RV dimensions and function, and PASP according to mortality status

Echocardiographic findings	Mortality (+) n=14	Mortality (-) n=73	p-Value
Right heart Dimensions:			
RA area (cm²)	22.50 [20.00-30.25]	22.00 [17.00-27.00]	.334
Basal RV diameter (mm)	44.00 [40.00-52.75]	41.00 [38.00-48.00]	0.161
TAD (mm)	41.00 [38.00-47.00]	38.00 [36.00-43.00]	0.080
TADi (mm/m²)	22.50 [19.25-23.75]	20.00 [18.00-22.00]	0.139
RV function :			
S' Velocity (cm/s)	9.50±2.28	10.49±2.64	
TAPSE (mm)	15.79±3.24	18.16±3.86	
Tei	0.52 [0.48-0.68]	0.49 [0.40-0.60]	
RV FRs	33.85±13.06	39.92±11.88	
RVFWLS	-17.00 [-19.00—14.00]	-17.00 [-21.00—14.00]	
Pulmonary Hypertension :			
PASP (mmHg)	63.62±19.09	49.00±15.00	.341
TR velocity (m/s)	3.27 [2.90-3.70]	3.20 [2.90-3.70]	0.763
RAP (mmHg)	15.00 [13.75-20.00]	10.00 [5.00-15.00]	0.027
RV–Pulmonary Arterial Coupling Index			
TAPSE/PASP	0.28 [0.24–0.31]	0.31 [0.23–0.40]	0.186
Severe TR	3/14 (21.4%)	6/73 (8.2%)	0.155
IVC diameter	25.00 [24.00-26.00]	23.00 [22.00-25.00]	0.096
Collapsibility			
Compliant	1 (7.1.0%)	27 (37.0%)	0.031
Non-compliant	13 (92.9%)	46 (63.0%)	

RA: Right atrium, RV: Right ventricular, TAD: Tricuspid annular diameter, TADi: Indexed tricuspid annular diameter TAPSE: Tricuspid annular plane systolic excursion, PASP: Pulmonary artery systolic pressure, TR: Tricuspid regurgitation, RAP: Right atrial pressure.

In-hospital management and discharge therapy according to mortality status

In-hospital management according to mortality status is presented in Table VIII, while discharge therapy is summarized in Table IX. Patients who died received significantly higher doses of loop diuretics during hospitalization (1000 [547.5–1500] vs 240 [120–500] mg, p<0.001) and more frequently required catecholamines (50.0% vs 12.3%, p=0.003) and RRT (28.6% vs 4.1%, p=0.012). Fluid intake was also significantly lower among non-survivors. Other in-hospital treatments, including respiratory support and thiazide diuretics, were comparable between groups. At discharge, most patients received GDMT, including beta-blockers, ACE inhibitors or ARBs, mineralocorticoid receptor antagonists, and SGLT2 inhibitors, with no significant differences between survivors and non-survivors except for higher loop diuretic doses in the mortality group.

Table 8. In-hospital management according to mortality status

Therapeutic intervention	Mortality (+) n=14	Mortality (-) n=73	p-Value
Respiratory support	9 (64.3%)	31 (42.5%)	0.216
Loop diuretic :			
Dose (mg)	1000.00 [547.50-1500.00]	240.00 [120.00-500.00]	<0.001
Treatment duration (Days)	18.00 [9.25-25.5]	11.00 [6.00-17.50]	0.061
Thiazide diuretics	6 (42.9%)	13 (17.8%)	0.071
Acetazolamide	1 (7.1%)	4 (5.5%)	1.000
Catecholamines	7 (50.0%)	9 (12.3%)	0.003
Renal replacement therapy	4 (28.6%)	3 (4.1%)	0.012
Fluid intake (mL)	250.00 [0.00–500.00]	1000.00 [500.00–1000.00]	<0.001

Table 9. Discharge characteristics and medical therapy according to rehospitalisation status

Parameter	Mortality (+) n=14	Mortality (-) n=73	p-Value
Loop diuretics	7 (100%)	73 (100%)	1.000
Dose loop diuretics	250.00 [250.00-562.50]	80.00 [40.00-250.00]	0.027
Beta-blockers	7/7 (100.0%)	67/73 (91.8%)	1.000
ACEi/ARBs	4/7 (57.1%)	38/73 (52.1%)	1.000
ARNi	0/7 (0.0%)	5/73 (6.8%)	1.000
MRA	3/7 (42.9%)	20/73 (27.4%)	0.404
ISGLT2	4/7 (57.1%)	51/73 (69.9%)	0.671

ACEi : Angiotensin converting enzyme inhibitors, ARBs: Angiotensin II receptor blockers, ARNi: Angiotensin receptor neprilysin inhibitor, MRA: Mineralocorticoid receptor antagonist, SGLT2i: Sodium-glocose cotransporter-2 inhibitors

Multivariable analysis

Multivariable logistic regression analysis for mortality is presented in Table X. Among the variables included in the model, higher serum creatinine levels at 48 hours (OR 3.125, 95% CI 2.648–15.047, p=0.021), lower UNa levels (OR 5.619, 95% CI 1.678–18.811, p=0.005), and reduced tricuspid annular plane systolic excursion (TAPSE) (OR 4.708, 95% CI 1.538–5.423, p=0.002) emerged as independent predictors of mortality. Other variables, including age, CKD, NT-proBNP, haemoglobin levels, and in-hospital treatment variables, were not independently associated with mortality in the multivariable model.

Table 10. Multivariable logistic regression analysis for mortality

Variable	OR	95% CI	p-Value
Age	1.269	0.982-2.119	0.161
CKD	3.995	1.149-6.638	0.996
Hourly urine output (mL/H)	0.985	0.970-1.000	0.080
NT-proBNP	2.350	1.000-8.227	0.145
HgB (g/dl)	0.650	0.400-1.040	0.074
Urea admission (mmol/L)	1.050	0.990-1.110	0.085
sCr admission (umol/L)	1.010	1.001-1.020	0.067
sCr 48H (umol/L)	3.125	2.648-15.047	0.021
ClCr 48H (mL/min)	0.900	0.810-1.000	0.054
NaU	5.619	1.678-18.811	0.005
Lactates ≥2 mmol/L	3.200	0.890-11.500	0.073
TAPSE	4.708	1.538-5.423	0.002
RAP (mmHg)	1.059	0.887-1.264	0.529
Furosemide dose 24H (mg)	1.003	1.002-1.103	0.184
Loop diuretics duration (days)	1.003	0.998-1.009	0.190
Catecholamines	1.560	0.300-8.010	0.595
Renal replacement therapy	2.900	0.880-9.520	0.080
Discharge loop diuretics dose (mg)	1.002	1.000-1.005	0.081

OR: Odds ratio, 95% CI: Confidence interval, CKD: Chronic kidney disease, NT-proBNP: N-terminal pro-B-type natriuretic peptide HgB: Haemoglobin, sCr: Serum creatinine, ClCr: Creatinine clearance, NaU: Urinary sodium, TAPSE: Tricuspid annular plane systolic excursion, RAP: Right atrial pressure.

Predictive performance of UNa for mortality in AHF

ROC curve analysis showed good predictive performance of UNa for mortality with area under the curve (AUC) of 0.82. The optimal cut-off value was 46 mmol/L, corresponding to a sensitivity of 64% and a specificity of 88%. The predictive performance of UNa, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), is summarized in Table XI, and its overall discriminatory ability is illustrated by the ROC curve shown in Figure 3.

Table 11. Predictive performance of low UNa for prediction of mortality

Variable	Sensitivity	Specificity	PPV	NPV
UNa ≤46 mmol/L	64.3%	87.7%	50.0%	92.8%

UNa: Urinary sodium, PPV: positive predictive value; NPV: negative predictive value

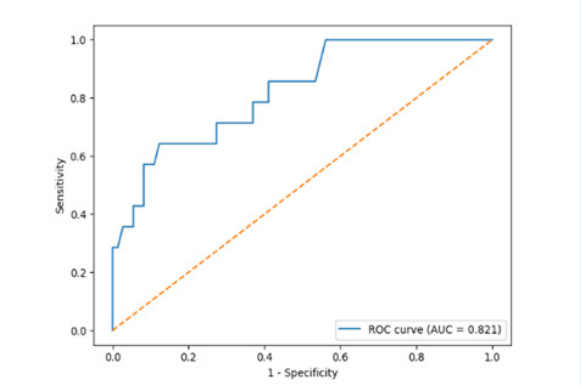

Figure 3. ROC curve of UNa for prediction of mortality (AUC = 0.82).

ROC: Receiver operating character, UNa: Urinary sodium, AUC: Area under the curve

DISCUSSION

In this prospective cohort of 87 patients admitted for AHF, the overall mortality rate reached 16.1% during follow-up, including 8.0% in-hospital deaths and additional events occurring at 3 and 6 months after discharge. Our findings highlight the prognostic value of early natriuretic response. In particular, lower UNa levels were strongly associated with mortality and emerged as an independent predictor in multivariable analysis. Urinary sodium also demonstrated good discriminative ability for mortality, with an AUC of 0.82, and a cut-off value of 46 mmol/L yielding a sensitivity of 64.3%, specificity of 87.7%, and a high NPV of 92.8%. In addition to impaired natriuretic response, markers of renal dysfunction at 48 hours and reduced RV systolic function, reflected by lower TAPSE values, were independently associated with mortality. Together, these findings emphasize the close interplay between renal congestion, diuretic response, and RV dysfunction in determining outcomes in patients with AHF.

The mortality rate observed in our cohort appears consistent with the range reported in contemporary HF registries, although direct comparisons should be interpreted cautiously due to differences in follow-up duration and patient characteristics. In the multinational EVOLUTION-HF study including more than 260,000 patients discharged after a first HF hospitalization, 1-year mortality reached 28%, reflecting the sustained vulnerability of patients following an HF admission [7]. Similarly, data from the ESC-HF-LT registry reported a 1-year mortality of 23.6% among patients hospitalized for AHF across European and Mediterranean centres [6]. Large pooled analyses have also confirmed the substantial burden of mortality following HF hospitalization. A systematic review and meta-analysis including more than half a million patients reported mortality rates of approximately 14% at 30 days and 29% at one year after discharge, emphasizing the persistent risk during the early post-discharge period [16].

Comparable patterns have been described in regional cohorts. Studies conducted in Sub-Saharan Africa have reported short-term mortality rates ranging from 3.7% to 19%, again highlighting the consistent prognostic impact of renal impairment [17].

Within the Tunisian context, the NATURE-HF registry documented an in-hospital mortality of 7.4% and a 1-year mortality of 22.8% among patients hospitalized for AHF [8]. Although our study involved a shorter follow-up period, the observed mortality trajectory appears broadly aligned with these regional data.

Our findings are in line with previous evidence highlighting the clinical relevance of UNa in AHF. A recent systematic review and meta-analysis including more than 8,700 patients demonstrated that higher UNa levels were associated with a more effective diuretic response, reflected by greater urine output, increased weight loss, and shorter hospital stay. Importantly, higher UNa was also linked to lower risks of renal function deterioration, rehospitalisation, and mortality during follow-up [18]. These data support the concept that early natriuretic response represents a key marker of effective decongestion and favourable clinical outcomes in patients with AHF. A systematic review and meta-analysis including 19 observational studies demonstrated that higher UNa levels after diuretic therapy were associated with greater urine output, more pronounced weight loss, shorter hospital stay, and significantly lower mortality during follow-up [12]. These observations reinforce the concept that urinary sodium reflects the effectiveness of decongestive therapy and may represent a simple marker of diuretic response and

clinical prognosis in AHF. In a prospective registry including 669 patients with AHF, Honda et al. reported that lower urinary sodium concentrations were associated with markers of haemodynamic severity, enhanced neurohormonal activation, and impaired diuretic response. Patients with reduced UNa exhibited less effective decongestion, a higher incidence of worsening renal function during hospitalization, and significantly poorer long-term outcomes. Importantly, UNa remained an independent predictor of adverse events during follow-up, supporting its role as an early indicator of diuretic resistance and adverse prognosis in AHF [19].

UNa has recently emerged as a promising biomarker to assess decongestion and guide diuretic therapy in patients hospitalized for AHF. Sodium excretion reflects the complex interaction between renal perfusion, neurohormonal activation and the pharmacological response to loop diuretics, making it a useful indicator of the effectiveness of decongestive treatment. Several studies have demonstrated that early assessment of spot UNa during the active phase of hospitalization provides important prognostic information and may identify patients with an inadequate natriuretic response and higher risk of adverse outcomes [20]. However, its interpretation remains highly dependent on the clinical context, including timing of measurement, volume status and ongoing diuretic therapy. Notably, previous investigations have shown that urinary sodium measured during the early decongestive phase carries prognostic significance, whereas measurements obtained at discharge appear to have limited predictive value for subsequent mortality or HF rehospitalization [20].

More recently, interest has grown in using UNa to guide diuretic titration strategies. A systematic review and meta-analysis evaluating urine sodium-guided diuresis suggested that this approach may enhance short-term natriuresis and diuresis and potentially improve renal safety, although its impact on longer-term clinical outcomes remains uncertain. Together, these findings support the concept that urinary sodium represents a dynamic marker of congestion and diuretic responsiveness rather than a standalone prognostic biomarker, and its clinical utility should therefore be interpreted within the broader haemodynamic and therapeutic context of AHF [21].

In a prospective study by Martens et al., serial measurements of spot UNa in patients with CHF demonstrated that individuals who subsequently developed acute decompensated HF had persistently lower UNa concentrations and exhibited a further decline in UNa levels in the week preceding hospitalization. Importantly, this reduction occurred before overt clinical deterioration, suggesting that changes in UNa may precede symptomatic congestion and provide early pathophysiological insights into impending decompensation. Moreover, UNa retained its discriminatory capacity for detecting AHF events even after adjustment for established biomarkers such as NT-proBNP and renal function indices. These observations support the concept that UNa reflects early alterations in renal sodium handling and congestion dynamics in HF, reinforcing its potential role as a clinically relevant marker of decongestive status [9].

CONCLUSION

In patients with AHF, UNa represents a simple and readily available biomarker reflecting the effectiveness of decongestive therapy and renal sodium handling. In the present study, lower UNa levels were significantly associated with an increased risk of short-term all-cause mortality, suggesting that impaired natriuretic response may identify patients with more severe congestion and poorer prognosis. These findings reinforce the clinical relevance of UNa as an indicator of diuretic responsiveness and congestion status in AHF. Future prospective studies are warranted to determine optimal UNa thresholds and to clarify its potential role in guiding individualized decongestive strategies and improving risk stratification in this population.

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