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Original Article

Influence of potassium levels on one-year outcomes in elderly patients with acute heart failure

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ABSTRACT

Background: Abnormal serum potassium levels (K^+) in patients with heart failure (HF) relate to worse prognosis. We evaluated whether admission K^+ levels predict 1-year outcomes in elderly patients admitted for acute HF.
Methods: We evaluated 2865 patients aged > 74 years from the RICA Spanish Heart Failure Registry, classified according to admission serum K^+ levels: hyperkalemia (> 5.5 mmol/L), normokalemia (3.5–5.5 mmol/L) and hypokalemia (< 3.5 mmol/L). We explored whether K^+ levels were significantly associated with one-year all-cause mortality or hospital readmission and their combination.
Results: Mean admission K^+ value was 4.3 ± 0.6 mmol/L; 97 patients (3.38%) presented with hyperkalemia and 174 (6.06%) with hypokalemia. Overall, 43% of the patients died or were readmitted for HF during the follow-up period; the risk was higher for those with hyperkalemia (59% vs 41% in hypokalemic patients). The HR for one-year mortality was 1.43 (p = .073) and 1.67 for readmissions (p = .007) when K^+ was > 5.5 mmol/L and 1.08 (p = .618) and 0.90 (p = .533) respectively for K^+ < 3.5 mmol/L. The HR for the combined outcome was 1.59 (1.19–2.13); p = .002 in hyperkalemic patients and 0.96 (0.75–1.23); p = .751in hypokalemic patients. Multivariate analysis showed a significant association of admission K^+ values > 5.5 mmol/L with the combined outcome of mortality and readmission (HR 1.15 [95% CI 1.04–1.27], p = .008).
Conclusion: In patients hospitalized for decompensated HF, admission hyperkalemia predicts a higher mid-term risk for HF readmission and mortality, probably related to the significant higher risk of readmission.

1. Introduction

Heart failure (HF) is one of the most common diseases worldwide due to its high prevalence and an incidence that increases with age [1,2]. The presence of HF is associated with significant morbidity and mortality [3]. Acute HF (AHF) events remain a major challenge in medical practice due to their high incidence and associated mortality [4], although in recent years, the short-term prognosis of AHF seems to be improving in terms of in-hospital and 30-day readmission/mortality rates [5].

Since most HF patients are elderly [6], comorbidities and their complications usually occur alongside AHF, significantly worsening the HF prognosis [2]. Moreover, polypharmacy is also very prevalent, which further increases the risk for HF readmission or all-cause mortality [7].

Electrolyte imbalances are one of the most prevalent complications in patients with AHF. Abnormal sodium (Na) levels in serum are common and have been thoroughly studied [8–10]. However, the role of hyperkalemia and hypokalemia upon admission, as predictors of adverse outcomes after an episode of AHF, has not been properly addressed. Arrhythmogenicity, in particular ventricular arrhythmias which may lead to cardiac arrest, is the most common complication

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resulting from abnormal K^+ levels [11,12]. Some studies have focused, with conflicting results, on the role of K^+ abnormalities in patients with chronic HF [13–16], but data on the short and mid-term prognosis in AHF patients with hyper- or hypokalemia on admission are scarce [17–20]. And, most important, there is a paucity of data regarding the role of K^+ abnormalities in the "real-life" predominant subset of elderly AHF patients. To fill this gap in knowledge, we designed a study focused on a cohort of unselected elderly patients discharged after an episode of AHF. In detail, we aimed at investigating whether an episode of AHF presenting with abnormal admission serum K^+ values (hyperkalemia or hypokalemia) associate with higher mid-term (1-year) risk of mortality or readmission when the focus of the analysis is restricted to HF patients aged 75 years of age or older as a main outcome, and also each one separately.

2. Methods

2.1. Patients

Patients were recruited from the National Registry of Heart Failure (RICA), an ongoing multicenter, prospective cohort survey supported by the Heart Failure-Working Group of the Spanish Society of Internal Medicine (SEMI-IC). In brief, the RICA, which began in March 2008, is a comprehensive registry of all consecutive patients with AHF admitted to the internal medicine wards of 52 public and private hospitals across Spain (only the index admission is considered). Patients are included in the RICA registry if they are discharged alive (in-hospital deaths are excluded) after the episode of AHF, and then followed for 1 year, with visits at 3 and 12 months after inclusion. Previous studies detailing RICA procedures have been recently published [21,22]. HF patients are identified according to the diagnostic criteria of the European Society of Cardiology [23]. The ethics committee of the University Hospital "Reina Sofia", Córdoba, Spain, approved the overall protocol and all participating patients sign an informed consent before being included in the RICA cohort. For the purpose of this study, only patients aged 75 years or older admitted between March 2008 and March 2017 were selected from the registry. Fig. 1 shows the flow-chart of the patient's inclusion criteria. Data collection and follow-up upon admission, a comprehensive medical history and a detailed physical examination are conducted and recorded. Aggregate comorbidity is evaluated using the Charlson Comorbidity index, preadmission functional status using the Barthel index, and cognitive status using the Pfeiffer questionnaire.

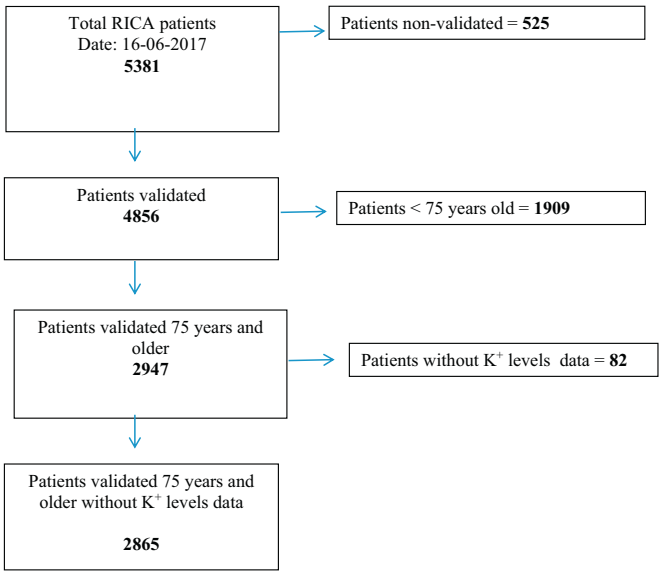

Fig. 1. Flow-chart of the patient's inclusion criteria.

Admission laboratory data (including serum levels of creatinine, urea, uric acid, glucose, sodium, potassium, natriuretic peptides and hemoglobin) are recorded. Clinical complications experienced during the index admission, and HF-related drug prescriptions at discharge are also registered. For the purpose of this study, all patients for whom laboratory data were incomplete or who did not have an echocardiographic examination performed during the index admission were excluded. Patients with a diagnosis of primary pulmonary hypertension, those deemed unable to cooperate with follow-up procedures (due to inability to schedule outpatient follow-up or expected survival of < 3 months), and those who refused to participate in the study or did not sign the informed consent were also excluded. In-hospital treatment decisions, timing of discharge and discharge medications were not prespecified and left to the attending physicians' discretion – the physicians were, however, aware that these patients were being included in the RICA registry. The estimated glomerular filtration rate (eGFR) was calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) equation, whose formula is: eGFR (mL/min/1.73 m^2) = 186.3 × (serum creatinine)$^{-1.154}$ × (age)$^{-0.203}$ × (1.212 if black race) × (0.742 if female).

For the outcome analyses, AHF patients were categorized into 3 categories according to admission plasma K^+ level status: hyperkalemia, defined as K^+ > 5.5 mmol/L (1 mmol/L = 1 mEq/L), normokalemia (3.5–5.5 mmol/L), and hypokalemia (< 3.5 mmol/L).

2.2. Primary outcomes

The primary endpoint was the combined outcome of readmission due to AHF or all-cause mortality within the first year of follow-up after the index admission discharge.

2.3. Statistical analysis

A descriptive analysis of the sample was performed. Patients were divided into 3 groups according to the aforementioned admission K^+ categories, and the baseline characteristics of both groups were compared using the ANOVA and Chi-square tests for quantitative and categorical variables respectively. Logistic regression analysis was performed to detect which baseline variables were associated with admission K^+ levels > 5.5 or < 3.5 mmol/L. All-cause mortality, HF-related readmissions, and their combination after 1 year were analyzed in the 3 groups of patients, and Kaplan-Meier curves of accumulated events were built to observe the prognostic differences between the 3 groups. A multivariate Cox analysis of logistic regression for mortality under the backward conditional method was performed including the variables that, in the univariate analysis, showed a statistically significant relation with the probability of readmission and/or death. The variables initially included in the multivariate analysis are those that present a level of significance lower than 0.1 in the univariate analysis and that, in addition, have a non-response percentage lower than 10%. The multivariate model is estimated in steps until the significant ones are retained.

The level of statistical significance was set at $p < .05$. For the data analysis, the Statistical Package for Social Sciences (SPSS) program (version 21.0, SPSS Inc. Chicago, IL, USA) was used.

3. Results

3.1. Baseline

A total of 2865 patients aged 75 or more were finally included, with a mean age of 83years; 57% were women. The mean admission K+ for the entire cohort was 4.3 ± 0.6mmol/L. Fig. 2 shows patient distribution according to their admission K+ values. In total, 97 patients (3.38%) presented with hyperkalemia and 174 (6.06%) with hypokalemia, while the remaining 2594 (90.5%) had admission K+ values

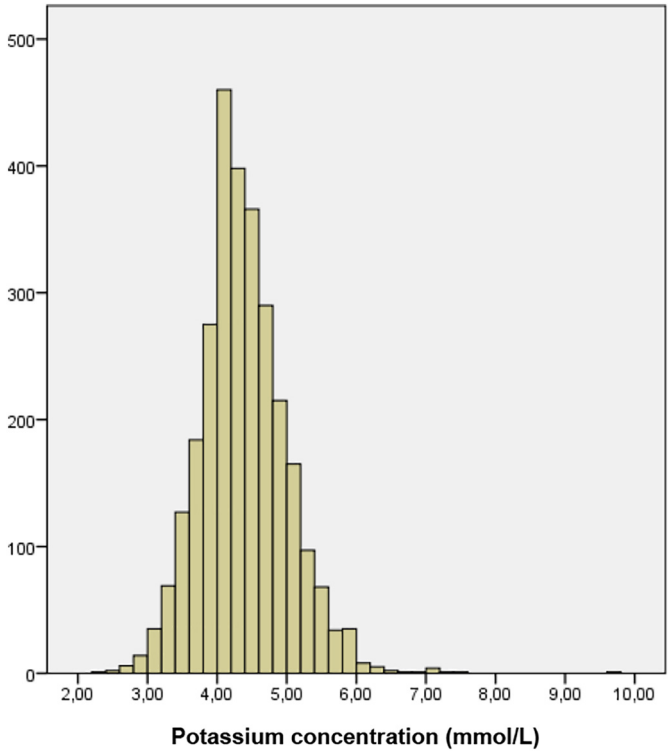

Fig. 2. Frequency (number of patients) of K^+ levels (mmol/L) at admission.

within normal range.

Table 1 shows the characteristics of the study cohort population according to the 3 pre-defined categories of admission K^+ values. A significantly higher prevalence of diabetes and dyslipidemia, higher comorbidity and lower pre-admission Barthel index were observed among hyperkalemic patients. Admission laboratory values also differed significantly between hyperkalemic (higher creatinine, urea and glucose) and hypokalemic patients (hyponatremia). Finally, preadmission use of thiazides was significantly higher among patients who were admitted with hypokalemia, and lower (also significantly) among those admitted with hyperkalemia. Although the difference was not significant, patients with normal K^+ on admission had a slightly shorter hospital stay than patients with abnormal K^+ values (7 days vs. 8 days).

3.2. Profile of hyperkalemic patients

Logistic regression analysis showed that admission $K^+ > 5.5$ mmol/L was significantly associated with higher concomitant creatinine (OR 1.54, 95% CI 1.20–1.97; $p < .001$) and urea values (OR 1.01, 95% CI 1.01–1.02; p < .001), lower sodium values (OR 0.95, 95% CI 0.92–0.99; $p = .012$), a higher prevalence of preadmission use of angiotensin-converting enzyme inhibitors (ACEI) (OR 1.03, 95% CI 1.03–2.59; $p = .038$) and a lower discharge prescription of thiazides (OR 0.31, 95% CI 0.11–0.89; $p = .030$).

3.3. Profile of hypokalemic patients

Logistic regression analysis showed a significant association of low admission K+ with a lower prevalence of preadmission dyslipidemia (OR 0.70, 95% CI 0.50–0.98; $p = .04$), lower admission urea (OR 0.99, 95% CI 0.98–0.99; < 0.001), lower admission glucose values (OR 0.99, 95% CI 0.98–1; $p = .004$), and a higher prevalence of preadmission thiazide use (OR 1.75, 95% CI 1.08–2.84; $p = .022$).

3.4. Outcomes (Table 1)

After 3 months of follow-up, 271 patients (10.1%) had died; at the 3-month time point, mortality was higher in the hyperkalemic group (17%) than in the hypokalemic group (7.9%), with no statistically significant differences ($p = .072$). By the end of the 12-month follow-up, global mortality had reached 25%; mortality figures remained higher for patients with admission $K^+ > 5.5$ mmol/L (33%) than for those with normal serum potassium values (25%) and patients with $K^+ < 3.5$ mmol/L (27%), and, once again, these figures did not reach statistical significance ($p = .176$).

The HR for one-year mortality was 1.43 (0.97–2.12; $p = .073$) in the group of patients with $K^+ > 5.5$ mmol/L and 1.08 (0.79–1.48; $p = .618$) in patients with $K^+ < 3.5$ mmol/L.

The overall HF readmission rate after 1 year of follow-up was 26%. This rate was slightly higher for the group of patients with hyperkalemia > 5.5 mmol/L (37%) than those with hypokalemia (23%), and did not reach statistical significance ($p = .056$).

The HR for one-year readmissions was 1.67 (1.15–2.43; $p = .007$) in the group of patients with $K^+ > 5.5$ mmol/L and 0.90 (0.65–1.26; $p = .553$) in patients with $K^+ < 3.5$ mmol/L.

3.5. Main outcome

HF readmissions and overall mortality could be assessed in a total of 2607 patients after 1 year of follow-up. In total, 1117 (43%) experienced either all-cause death or readmission due to a new episode of AHF during this period. These figures differed significantly but in opposite directions for hyperkalemic (59%) and hypokalemic (41%) patients. The HR for the combined outome of one-year mortality or readmissions was 1.59 (1.19–2.13); $p = .002$ in the group of patients with $K^+ > 5.5$ mmol/L and 0.96 (0.75–1.23); $p = .751$ in patients with $K^+ < 3.5$ mmol/L.

Fig. 3 shows the Kaplan-Meier curves for the main outcome according to the admission K^+ categories.

Table 2 shows the results of the univariate and multivariate analysis for the combined main outcome. Besides higher admission K^+ values, the following factors were associated in the univariate analysis with a higher risk of 1-year all-cause mortality or AHF readmission: age, dyslipidemia, Charlson, Barthel and Pfeiffer indexes, body mass index, systolic and diastolic blood pressure, hemoglobin, (eGFR), creatinine, urea, glucose, uric acid, left ventricular ejection fraction, NYHA class, HF etiology, and treatment with angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB); beta-blockers, and mineralocorticoid receptor antagonists (MRA).

In the Cox multivariate analysis, admission K^+ values retained the association with 1-year all-cause mortality or AHF readmissions (HR 1.15 [95% CI 1.04–1.27], $p = .008$). In addition, the following variables were also related with an independent increased risk of death or readmission: dyslipemia, Charlson, Barthel and Pfeiffer index, body mass index, systolic blood pressure, hemoglobin, eGFR, urea, NYHA class, HF etiology (ischemic and valvular), and treatment at discharge with ACEI/ARB, beta blockers, and MRA.

4. Discussion

Our main result is that in elderly patients with AHF, the presence of hyperkalemia at admission is a significant and independent marker of worse outcomes: in particular, a significant relationship was found between admission hyperkalemia and the combined outcome of one-year all-cause death or HF readmission. This relationship remained significant for readmission alone, but not for mortality. Instead, admission hypokalemia lacked association with any of those outcomes.

The overall admission serum K^+ in our cohort was 4.3 mmol/L, between 4.25 mmol/L for AHF [24] and 4.5 mmol/L for chronic HF [16]. Few AHF patients (3.38%) presented with hyperkalemia at

Table 1
Patient baseline characteristics according to admission K^+ values. Mortality and readmissions during follow-up according to admission K+ values.

	N	K^+ < 3.5 mmol/L (*n* = 174)	K^+ 3.5–5.5 mmol/L (*n* = 2594)	K^+ > 5.5 mmol/L (*n* = 97)	P
Age (years)	2865	83 (80–86)	83 (80–86)	82 (79–86)	0.545
Sex (female)	2865	109 (63%)	1483 (57%)	51 (53%)	0.231
Hypertension	2865	158 (91%)	2280 (88%)	83 (86%)	0.393
Diabetes mellitus	2865	74 (43%)	1398 (54%)	60 (62%)	0.004
Smoking	2865	46 (26%)	821 (32%)	37 (38%)	0.131
Alcohol	2865	26 (15%)	345 (13%)	14 (14%)	0.793
Dyslipidemia	2865	65 (37%)	1257 (48%)	51 (53%)	0.012
Atrial fibrillation/flutter	2865	117 (67%)	1729 (67%)	59 (61%)	0.479
Liver disease	2865	11 (6.3%)	113 (4.4%)	1 (1.0%)	0.124
Mean eGFR ml/min	2865	63 (47–79)	53 (38–70)	37 (26–52)	< 0,001
Charlson index (points)	2865	2.0 (0.0–4.0)	2.0 (1.0–4.0)	4.0 (3.0–5.0)	< 0,001
Barthel index (points)	2863	90 (60–100)	90 (65–100)	80 (55–95)	0.041
Pfeiffer index (points)	2596	1.0 (0.0–3.0)	1.0 (0.0–3.0)	1.0 (0.0–3.0)	0.613
BMI (kg/m2)	2865	27.0 (24.1–30.7)	27.9 (24.8–31.3)	27.6 (24.2–31.6)	0.123
SBP (mmHg)	2865	135 (115–160)	136 (120–154)	140 (123–155)	0.689
DBP(mmHg)	2865	75 (64–87)	73 (63–84)	75 (63–83)	0.414
Hemoglobin (g/dl)	2865	12.4 (10.9–13.6)	12.0 (10.7–13.2)	11.2 (9.9–12.8)	0.003
Creatinine(mg/dl)	2865	1.0 (0.8–1.3)	1.2 (0.9–1.6)	1.7 (1.3–2.1)	< 0,001
Urea (mg/dl)	2651	49 (37–69)	62 (46–86)	98 (72–130)	< 0,001
Sodium (mEq/L)	2865	141 (137–143)	139 (136–142)	137 (133–140)	< 0,001
Potassium (mEq/L)	2865	3.2 (3.1–3.4)	4.4 (4.0–4.7)	6 (5.7–6.0)	< 0,001
Glucose(mg/dl)	2659	110 (92–133)	119 (97–157)	124 (96–179)	< 0,001
Uric acid (mg/dl)	1743	7.6 (6.0–9.3)	7.9 (6.3–9.6)	8.5 (6.9–10.0)	0.106
BNP (pgr/ml)	372	563 (331–1776)	656 (352–1180)	1026 (362–3294)	0.736
LVEF (%)	2864	57 (45–65)	55 (41–64)	57 (45–66)	0.103
LVEF > 45%	2864	131 (75%)	1883 (73%)	76 (78%)	0.357
NYHA					
I	2828	16 (9.4%)	178 (6.9%)	3 (3.2%)	0.162
II	2828	97 (57%)	1397 (55%)	55 (58%)	0.705
III	2828	55 (32%)	901 (35%)	33 (35%)	0.727
IV	2828	3 (1.8%)	86 (3.4%)	4 (4.2%)	0.459
Etiology					
Ischemic	2836	41 (24%)	684 (27%)	24 (25%)	0.687
Hypertensive	2836	77 (45%)	1039 (40%)	40 (42%)	0.529
Valvular	2836	32 (19%)	486 (19%)	15 (16%)	0.717
Other	2836	22 (13%)	359 (14%)	17 (18%)	0.522
Treatment at admission					
ACE inhibitors	2865	47 (27%)	765 (29%)	33 (34%)	0.479
ARBs	2865	37 (21%)	580 (22%)	24 (25%)	0.804
IECA/ARA	2865	83 (48%)	1324 (51%)	55 (57%)	0.364
Beta-Blocking agents	2865	64 (37%)	975 (38%)	41 (42%)	0.625
Loop diuretics	2865	114 (66%)	1628 (63%)	62 (64%)	0.752
Thiazides	2865	20 (11%)	174 (6.7%)	3 (3.1%)	0.018
Aldosterone antagonists	2865	24 (14%)	431 (17%)	20 (21%)	0.346
Length of stay, days	2860	8.0 (5.0–13.0)	7.0 (5.0–11.0)	8.0 (5.0–12.0)	0.050
Treatment at discharge					
ACEI	2865	66 (38%)	1066 (41%)	35 (36%)	0.455
ARBs	2865	45 (26%)	696 (27%)	21 (22%)	0.512
ACEI/ARA	2865	110 (63%)	1742 (67%)	55 (57%)	0.063
Beta blockers	2865	97 (56%)	1455 (56%)	57 (59%)	0.868
Loop diuretics	2865	152 (87%)	2259 (87%)	78 (80%)	0.158
Thiazides	2865	26 (15%)	246 (9.5%)	4 (4.1%)	0.011
MRAs	2865	50 (29%)	725 (28%)	21 (22%)	0.380
Outcomes					
All-cause mortality at 3 months	2684	13 (7.9%)	244 (10%)	14 (17%)	0.072
All-cause mortality at 1 year	2572	42 (27%)	578 (25%)	26 (33%)	0.176
HF readmission at 1 year	2607	36 (23%)	601 (25%)	29 (37%)	0.055
HF readmission and/or all-cause mortality at 1 year	2607	65 (41%)	1005 (42%)	47 (59%)	0.010

ACEI: angiotensin-converting enzyme inhibitors; ARA: angiotensin II receptor antagonists; ARBs: angiotensin II receptor blockers; BMI: body mass index; BNP: brain natriuretic peptide; CKD: chronic kidney disease; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate;HF: heart failure; LVEF: left ventricular ejection fraction; MRAs: mineralocorticoid receptor antagonists; NYHA: New York Heart Association; SBP: systolic blood pressure.

admission, a figure similar to the 4% reported by Hoss et al. (K^+ > 5.4 mmol/L) in chronic HF patients [16]. Higher percentages (9%) have been reported when a lower, cut-off value of > 5 mmol/L for hyperkalemia is used in AHF [19].

Comorbidities, such as chronic kidney disease or diabetes mellitus and, especially, the use of renin-angiotensin-aldosterone system inhibitors, place patients with HF at a higher risk for developing hyperkalemia [17,25–26]. Our logistic regression analysis confirm these findings; hyperkalemia was associated with significantly impairment of renal function (poor higher creatinine and urea serum levels), and lower serum sodium values on admission. With respect to the important role of medications according serum potassium values we found also a higher prevalence of preadmission use of ACEI and a lower discharge prescription of thiazides in the hyperkalemic group.

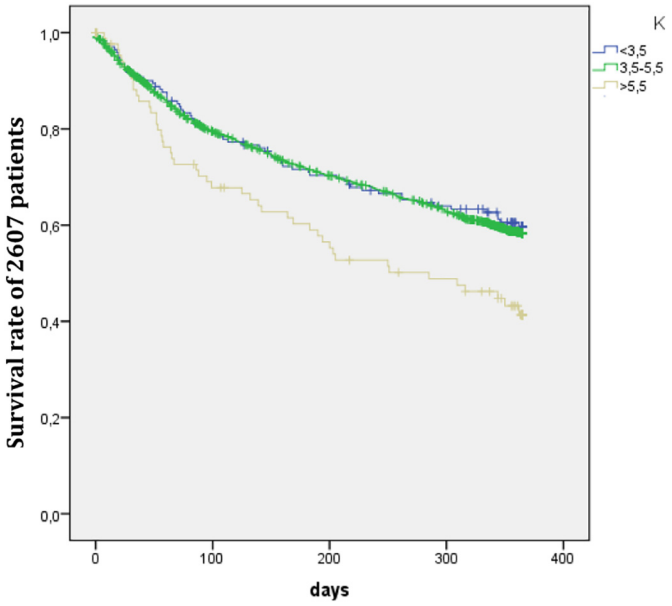

Fig. 3. Kaplan Meier curves for the main outcome (cumulative mortality or AHF) readmission stratified according to low (< 3.5 mmol/L), normal, or high (> 5.5 mmol/L) admission K+ values. Log-rank ratio *p*-value = .007.

In our cohort, a total of 174 (6.06%) patients had hypokalemia, similar to the prevalence reported by Tromp et al. [19], but this rate was much higher than the 1.7% found by Hoss et al. [16]. Hypokalemia is common in HF patients, often due to a defect in Na+/K+ -ATPase activity and intracellular shift of K, caused by oxidative stress and neurohormonal activation, but it can also be a side effect of diuretic use [27]. In our study, low K^+ values were indeed associated with higher preadmission thiazide use.

Regarding hyperkalemia and AHF outcomes, this study shows that admission serum K^+ levels > 5.5 mmol/L were significantly associated with higher mortality and HF readmissions. The main outcome of combined mortality and readmissions for AHF was even more prevalent in hyperkalemic patients. Several authors have reported that normal-high K^+ levels in HF patients are clinically safe and confer a similar clinical risk to normal K^+ levels [14,15]. However, data from the PROTECT and COACH trials show a univariate linear association of admission serum K^+ levels with 3-month mortality risk, although this association was not maintained after multivariate analysis [19].

In contrast to the report by Hoss et al. [16] on octogenarian patients with K^+ < 3.5 mmol/L, hypokalemia did not contribute to a significantly worse prognosis for mortality, readmissions, or the combined event in our cohort. A substudy of the Digitalis Investigation group trial in 3598 patients (mean age, 72 years) also reported an association between lower or low-normal (3.5–3.9 mmol/L) K^+ serum values with mortality, but not with readmissions [28].

Recently data from the Danish National registry investigators reported a U-shaped relationship between serum K^+ and short-term risk

Table 2
Univariate and multivariate Cox analysis of risk for 1-year mortality or AHF readmission.

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Age (years)	1.03 (1.01–1.04)	< 0.001	N.S.	
Sex (female)	1.07 (0.95–1.21)	0.243	N.S.	
Hypertension	1.11 (0.92–1.33)	0.295	N.S.	
Diabetes mellitus	1.06 (0.94–1.19)	0.344	N.S.	
Dyslipidemia	1.17 (1.04–1.31)	0.010	1.17 (1.02–1.33)	0.023
Atrial fibrillation/flutter	1.08 (0.95–1.22)	0.247	N.S.	
Charlson index (points)	1.10 (1.07–1.12)	< 0.001	1.04 (1.02–1.07)	0.001
Barthel index (points)	0.99 (0.99–0.99)	< 0.001	0.99 (0.99–1.00)	< 0.001
Pfeiffer index (points)	1.13 (1.10–1.15)	< 0.001	1.08 (1.04–1.11)	< 0.001
BMI (Kg/m2)	0.98 (0.96–0.99)	< 0.001	0.98 (0.97–0.99)	0.002
SBP (mmHg)	1.00 (0.99–1.00)	0.001	1.00 (0.99–1.00)	0.040
DBP(mmHg)	0.99 (0.99–1.00)	< 0.001	N.S.	
Hemoglobin (g/dl)	0.93 (0.90–0.95)	< 0.001	N.S.	
eGFR (ml/min)	0.99 (0.99–0.99)	< 0.001	0.99 (0.99–1.00)	0.005
Creatinine (mg/dl)	1.25 (1.18–1.33)	< 0.001	N.S.	
Urea (mg/dl)	1.01 (1.00–1.01)	< 0.001	1.00 (1.00–1.00)	0.028
Sodium (mEq/L)	0.98 (0.97–0.98)	< 0.001	N.S.	
Potassium (mEq/L)	1.24 (1.13–1.36)	< 0.001	1.15 (1.04–1.27)	0.008
LVEF (%)	0.99 (0.99–1.00)	0.009	N.S.	
LVEF > 45%	0.86 (0.76–0.98)	0.023	N.S.	
NYHA III-IV	1.56 (1.39–1.76)	< 0.001	1.29 (1.13–1.47)	< 0.001
Etiology				
• Ischemic	1.21 (1.07–1.38)	0.003	1.24 (1.06–1.45)	0.009
• Hypertensive	0.78 (0.69–0.89)	< 0.001	N.S.	
• Valvular	1.36 (1.18–1.56)	< 0.001	1.40 (1.18–1.64)	< 0.001
Treatment at discharge				
• ACEI	0.91 (0.80–1.02)	0.108	N.S.	
• ARBs	0.86 (0.76–0.99)	0.032	N.S.	
• ACEI/ARA	0.78 (0.69–0.88)	< 0.001	0.87 (0.76–0.99)	0.041
• Betablockers	0.85 (0.75–0.95)	0.006	0.84 (0.73–0.96)	0.009
• Loop diuretics	1.11 (0.91–1.35)	0.308	N.S.	
• Thiazides	1.06 (0.87–1.28)	0.553	N.S.	
• Aldosterone antagonists	1.16 (1.02–1.31)	0.024	1.16 (1.01–1.33)	0.037

NS: non-significant.
ACEI: angiotensin-converting enzyme inhibitors; ARA: angiotensin II receptor antagonists; ARBs: angiotensin II receptor blockers; BMI: body mass index; BNP: brain natriuretic peptide; CKD: chronic kidney disease; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; MRAs: mineralocorticoid receptor antagonists; NYHA: New York Heart Association; SBP: systolic blood pressure.

of death (90 days) in patients with chronic HF emphasizing the prognostic role of to have potassium level within the lower and upper levels of the normal serum potassium range [29].

In a single-center, prospective, observational study of 2164 consecutively discharged patients after an admission for AHF, Nuñez et al. [20] investigated the long-term prognostic significance of dynamic serum K+ changes, instead of just using the baseline admission value. This study highlights the relevance of close monitoring serum K+ after the episode of AHF: potassium dynamics analysis reveal that persistent follow-up hypokalemia or hyperkalemia identify a subset of patients with mortality risks higher than those found among patients who persisted with or returned to normokalemia.

Our study has several limitations. Firstly, as mentioned in the methods section, patients who die during the index admission are not included in the RICA registry, so their admission data are not available for the analysis. Secondly, biomarkers were available in only a subgroup of our patients. Thirdly, no data were retrieved either on the progress of K^+ levels during the index admission and at the time of discharge, or on K-modifying therapies administered, which could significantly influence patients' prognosis. In fourth place, the lack of association of hypokalemia with mortality might be underestimated due to the relatively small number of patients who presented with low admission potassium levels. And last, other than recording treatment at discharge, we did not analyze how post-discharge management or intervening incidents may have modulated mortality risks. We would finally remark that the applicability of our results should be put in context: our HF patient sample is made up of elderly subjects (mean age 83 years) with a high prevalence of preserved LV ejection fraction (75%), atrial fibrillation (67%) and hypertension (88%)…

In conclusion, admission serum K^+ levels > 5.5 mmol/L confer a significant and independent risk of worse prognosis for the combined outcomes of death or HF readmission in elderly AHF patients, a relationship which seems mostly related to a greater number of readmissions. Our results emphasize the importance of K^+ values in elderly AHF patients and suggest that controlling K^+ promptly might lead to a reduction in adverse outcomes in this population.

Conflict of interest

None.

No author has any relationship with industry and financial associations from within the past 3 years that might pose a conflict of interest with the manuscript.

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The authors declare that there are no conflicts of interest.

Appendix A. RICA registry members

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