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SERUM POTASSIUM VARIABILITY PREDICTS SHORT-TERM ARRHYTHMIA RISK IN HEART FAILURE PATIENTS: A POST-DISCHARGE OBSERVATIONAL COHORT STUDY

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Abstract

Objective: To investigate whether serum potassium (K^+) variability during hospitalization for acute decompensated heart failure (ADHF) predicts 30-day arrhythmia readmissions, independent of absolute K^+ levels, and to identify high-risk subgroups.

Methods: This retrospective observational cohort study analyzed 300 patients. Serum K^+ variability was quantified as the standard deviation (SD) of serial measurements. The primary outcome was 30-day readmission for ECG-confirmed arrhythmia (atrial fibrillation, ventricular tachycardia, or sustained supraventricular tachycardia). Multivariable logistic regression adjusted for age, ejection fraction, renal function, diuretic dose, magnesium levels, and beta-blocker use.

Results: Among 300 patients (mean age 68 ± 10 years, 45% HFrEF), 60 (20%) were readmitted for arrhythmias. The arrhythmia group exhibited significantly higher K^+ variability (SD 0.45 ± 0.15 vs. 0.25 ± 0.10 mmol/L, p <0.001), with each 0.1 mmol/L SD increase associated with 40% higher adjusted odds of arrhythmia (aOR=1.4, 95% CI:1.2–1.7, p=0.001). Subgroup analyses revealed stronger associations in HFrEF (aOR=2.2, p=0.01) and hypomagnesemic patients (aOR=2.5, p=0.008). Beta-blocker use attenuated risk (aOR=0.5, p=0.02), while high-dose diuretics amplified it (aOR=2.5, p<0.001). Ventricular tachycardia occurred earlier post-discharge (median 10 vs. 14 days for atrial fibrillation).

Conclusion: Serum K^+ variability during ADHF hospitalization is an independent predictor of short-term arrhythmia risk, particularly in patients with HFrEF or hypomagnesemia. These findings advocate for protocolized K^+ stabilization, magnesium repletion, and beta-blocker optimization to reduce arrhythmia-related morbidity, especially in resource-limited settings.

Keywords: Serum potassium variability; Heart failure; Arrhythmia readmissions; Hypomagnesemia; Beta-blockers; Risk stratification

1. Introduction

Heart failure (HF) represents a global health burden, affecting over 64 million individuals worldwide, with acute decompensated heart failure (ADHF) accounting for nearly 1 million annual hospitalizations in the United States alone (Groenewegen et al., 2020). Despite advancements in guideline-directed medical therapy, 30-day readmission rates remain alarmingly high (20–25%), driven largely by arrhythmic complications such as atrial fibrillation (AF) and ventricular tachycardia (VT), which contribute to sudden cardiac death and prolonged morbidity (Ambrosy et al., 2014; Ponikowski et al., 2016). Serum potassium (K^+) homeostasis, a cornerstone of myocardial electrophysiology, is routinely monitored in HF management due to its critical role in maintaining cellular repolarization. However, current clinical paradigms prioritize the prevention of absolute hypokalemia (<3.5 mmol/L) or hyperkalemia (>5.0 mmol/L), while overlooking the potential

arrhythmogenic impact of within-normal fluctuations in serum K^+ (Weiss et al., 2017; Grodzinsky et al., 2020).

The myocardium's sensitivity to K^+ is governed by its influence on the resting membrane potential and action potential duration. Even minor perturbations in extracellular K^+ concentrations, as small as 0.5 mmol/L, alter the transmembrane K^+ gradient, increasing dispersion of repolarization and promoting ectopic activity (Szentadrassy et al., 2015). This vulnerability is amplified in HF patients, whose myocardium is structurally and electrically remodeled due to fibrosis, ion channel downregulation, and neurohormonal activation (Nattel et al., 2007). Concomitant therapies such as loop diuretics, while essential for decongestion, exacerbate electrolyte instability by promoting renal K^+ and magnesium (Mg^{2+}) wasting, further predisposing patients to arrhythmias (Ellison & Felker, 2017; Viering et al., 2021). Despite this pathophysiological interplay, no studies have systematically evaluated whether variability in serum K^+ during hospitalization—a simple, low-cost biomarker—predicts post-discharge arrhythmia risk. Current HF guidelines emphasize maintaining serum K^+ >4.0 mmol/L but lack specific recommendations on minimizing short-term K^+ fluctuations (McDonagh et al., 2021; Heidenreich et al., 2022). This oversight is clinically consequential, as small hospitals often lack access to advanced arrhythmia monitoring tools (e.g., implantable loop recorders), rendering prevention dependent on modifiable risk factors. Preliminary work by Aldahl et al. (2017) demonstrated that K^+ variability in critically ill patients correlates with mortality, yet this relationship remains unexplored in the HF population. Furthermore, hypomagnesemia—present in 30–50% of HF patients—may synergize with K^+ instability by impairing Na^+/K^+-ATPase activity, thereby exacerbating repolarization abnormalities (Viering et al., 2021; Hansen et al., 2022).

This study investigates the hypothesis that higher serum K^+ variability during ADHF hospitalization independently predicts 30-day arrhythmia readmissions, even after adjusting for absolute K^+ levels, renal function, and diuretic exposure. By leveraging routinely collected clinical data, we aim to identify a pragmatic biomarker to refine risk stratification and guide electrolyte management in HF patients, particularly in resource-limited settings. Our findings may inform protocols to narrow K^+ target ranges, optimize Mg^{2+} repletion, and prioritize high-risk patients for early post-discharge monitoring—a critical step toward reducing arrhythmia-related morbidity in this vulnerable population.

2. Methodology

2.1. Study Design and Population

This retrospective observational cohort study was conducted at GMC Srinagar and associated hospital serving a mixed urban and rural population. Consecutive patients admitted with a primary diagnosis of acute decompensated heart failure (ADHF) between January 2024 and December 2024 were screened for eligibility. ADHF diagnosis was confirmed using the 2021 European Society of Cardiology (ESC) Heart Failure Guidelines, which require the presence of typical symptoms (e.g., dyspnea, fatigue), signs (e.g., peripheral edema, elevated jugular venous pressure), and objective evidence of cardiac dysfunction (e.g., elevated natriuretic peptides or echocardiographic abnormalities) (McDonagh et al., 2021). Inclusion criteria comprised hospitalization for ≥3 days with ≥3 serum potassium (K^+) measurements and post-discharge follow-up within 30 days (clinic visit or readmission). Exclusion criteria included end-stage renal disease (eGFR <15 mL/min/1.73m² or ongoing dialysis), pre-existing arrhythmias (atrial fibrillation, ventricular tachycardia, or pacemaker dependency), and incomplete electrolyte or medication records. The final cohort consisted of 300 patients, stratified into two groups based on 30-day arrhythmia readmission status.

2.2. Data Collection and Variables

Data were extracted from electronic health records (EHRs) using a standardized protocol validated through pilot testing. Demographic variables included age, sex, body mass index (BMI), and smoking status (categorized as current, former, or never). Clinical parameters encompassed left ventricular ejection fraction (LVEF) measured via transthoracic echocardiography within 48 hours of admission,

classified as heart failure with reduced ejection fraction (HFrEF, LVEF ≤40%) or preserved ejection fraction (HFpEF, LVEF ≥50%), and New York Heart Association (NYHA) functional class at admission. Comorbidities such as hypertension, diabetes mellitus, and chronic kidney disease (CKD, defined as eGFR <60 mL/min/1.73m² using the CKD-EPI equation) were documented. Serum electrolyte data included all potassium (K^+) measurements obtained during hospitalization (mmol/L), with variability quantified as the standard deviation (SD) of serial values. Magnesium (Mg^{2+}) and calcium (Ca^{2+}) levels were recorded as the lowest concentrations during admission. Renal function was assessed using peak serum creatinine and eGFR. Medication use, including loop diuretic dose (converted to furosemide-equivalent daily dose), angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), beta-blockers, and mineralocorticoid receptor antagonists (MRAs), was catalogued.

2.3. Outcome Ascertainment

The primary outcome was 30-day readmission for ECG-confirmed arrhythmia, including atrial fibrillation (AF), ventricular tachycardia (VT), or sustained supraventricular tachycardia (SVT). Arrhythmias were verified by two independent cardiologists using 12-lead ECG or telemetry documentation, with discrepancies resolved by a third reviewer. Secondary outcomes included arrhythmia subtype and time-to-event (days from discharge to readmission).

2.4. Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range, IQR) based on normality, assessed via Shapiro-Wilk tests. Categorical variables were reported as frequencies (%). Group comparisons (arrhythmia vs. non-arrhythmia) employed Student's t-tests for normally distributed data, Mann-Whitney U tests for non-parametric data, and χ^2 tests for categorical variables. Univariable and multivariable logistic regression models evaluated associations between serum K^+ variability (per 0.1 SD increase) and 30-day arrhythmia risk. Adjusted models included covariates selected a priori based on clinical relevance: age, sex, LVEF, loop diuretic dose, magnesium level, eGFR, and beta-blocker use. Results were reported as odds ratios (OR) with 95% confidence intervals (CI). Subgroup analyses stratified by LVEF (HFrEF vs. HFpEF) and magnesium status (hypomagnesemia [<0.7 mmol/L] vs. normal) were conducted to explore effect modification. Time-to-event analyses utilized Kaplan-Meier curves with log-rank tests and Cox proportional hazards models to assess the relationship between K^+ variability quartiles and arrhythmia risk. Sensitivity analyses excluded patients with CKD or restricted the cohort to those with ≥4 K^+ measurements to evaluate robustness. Dose-response relationships were tested using trend analyses across K^+ variability quartiles. Statistical significance was defined as a two-tailed $p < 0.05$. Analyses were performed using R version 4.2.2 (R Foundation for Statistical Computing) and SPSS version 28 (IBM Corporation).

3. Results

3.1. Baseline Characteristics of the Study Population

The study cohort comprised 300 patients hospitalized with acute decompensated heart failure (ADHF), of whom 20% (n=60) experienced arrhythmia-related readmission within 30 days. Patients in the arrhythmia group were significantly older (72 ± 8 vs. 67 ± 11 years, p=0.003) and more likely to have heart failure with reduced ejection fraction (HFrEF, 70% vs. 38%, p<0.001). Notably, serum potassium (K^+) variability, quantified as the standard deviation (SD) of serial measurements, was markedly higher in the arrhythmia group (0.45 ± 0.15 vs. 0.25 ± 0.10 mmol/L, p<0.001), whereas average K^+ levels did not differ between groups (4.2 ± 0.3 vs. 4.1 ± 0.4 mmol/L, p=0.35). This underscores the clinical relevance of K^+ fluctuations rather than absolute values. The arrhythmia group also exhibited higher rates of hypomagnesemia (45% vs. 20%, p<0.001), high-dose diuretic use (55% vs. 18%, p<0.001), and chronic kidney disease (60% vs. 28%, p<0.001), suggesting a multifactorial pathophysiology linking electrolyte instability, neurohormonal activation, and renal dysfunction to

arrhythmogenesis. Beta-blocker use was significantly lower in the arrhythmia group (50% vs. 80%, p<0.001), aligning with their established role in reducing ventricular ectopy (Table.1).

Table 1: Baseline Characteristics of the Study Population

Variable	Total Cohort (n=300)	Arrhythmia Group (n=60)	Non-Arrhythmia Group (n=240)	p-value
Age (years)	68 ± 10	72 ± 8	67 ± 11	0.003
Male Sex	55%	65%	52%	0.08
HFrEF (LVEF ≤40%)	45%	70%	38%	<0.001
K+ Variability (SD)	0.30 ± 0.15	0.45 ± 0.15	0.25 ± 0.10	<0.001
Average K+ (mmol/L)	4.1 ± 0.4	4.2 ± 0.3	4.1 ± 0.4	0.35
Hypomagnesemia (<0.7 mmol/L)	25%	45%	20%	<0.001
High Diuretic Dose (>120 mg/day)	25%	55%	18%	<0.001
CKD (eGFR <60)	35%	60%	28%	<0.001
Beta-Blocker Use	75%	50%	80%	<0.001

3.2. Multivariable Logistic Regression for 30-Day Arrhythmia Risk

After adjusting for age, sex, ejection fraction, diuretic dose, magnesium levels, renal function, and beta-blocker use, serum K^+ variability emerged as an independent predictor of 30-day arrhythmia risk. Each 0.1 mmol/L increase in K^+ variability (SD) was associated with a 40% higher odds of arrhythmia (aOR=1.4, 95% CI: 1.2–1.7, p=0.001). Age (per 5-year increase: aOR=1.2, p=0.03) and HFrEF (aOR=2.1, p=0.002) further amplified risk, reflecting the vulnerability of older patients and those with structurally compromised myocardium to electrical instability. Hypomagnesemia (aOR=1.8, p=0.02) and high-dose diuretics (aOR=2.5, p<0.001) independently contributed to arrhythmia risk, likely through synergistic effects on Na^+/K^+-ATPase dysfunction and potassium wasting. Conversely, beta-blocker use was protective (aOR=0.5, p=0.02), consistent with their antiadrenergic and antifibrillatory properties. These findings highlight the interplay between modifiable electrolyte derangements, neurohormonal therapies, and intrinsic patient factors in post-discharge arrhythmia risk (Table.2).

Table 2: Multivariable Logistic Regression for 30-Day Arrhythmia Risk

Predictor	Adjusted Odds Ratio (aOR)	95% CI	p-value
K+ Variability (per 0.1 SD)	1.4	1.2–1.7	0.001
Age (per 5-year increase)	1.2	1.0–1.4	0.03
HFrEF	2.1	1.3–3.5	0.002
Hypomagnesemia	1.8	1.1–2.9	0.02
High Diuretic Dose	2.5	1.5–4.2	<0.001
Beta-Blocker Use	0.5	0.3–0.9	0.02

3.3. Subgroup Analysis of K^+ Variability and Arrhythmia Risk

Subgroup analyses revealed significant heterogeneity in the association between K^+ variability and arrhythmia risk. In patients with HFrEF, each 0.1 mmol/L increase in K^+ variability conferred a 120% higher odds of arrhythmia (aOR=2.2, 95% CI: 1.6–3.1, interaction p=0.01), whereas no significant association was observed in HFpEF (aOR=1.1, p=0.4). This disparity may reflect differences in myocardial substrate: HFrEF patients exhibit greater electrical remodeling (e.g., fibrosis, ion channel downregulation), rendering them more susceptible to repolarization abnormalities. Similarly,

hypomagnesemia potentiated the arrhythmogenic effect of K^+ variability (aOR=2.5 vs. 1.2 in normomagnesemic patients, interaction p=0.008), likely due to magnesium's role in stabilizing potassium channels and reducing delayed afterdepolarizations. These results advocate for targeted monitoring of K^+ stability in high-risk subgroups, particularly HFrEF patients with concurrent hypomagnesemia (Table.3).

Table 3: Subgroup Analysis of K+ Variability and Arrhythmia Risk

Subgroup	Adjusted OR (95% CI)	Interaction p-value
LVEF ≤40% (HFrEF)	2.2 (1.6–3.1)	0.01
LVEF ≥50% (HFpEF)	1.1 (0.8–1.5)	
Hypomagnesemia Present	2.5 (1.8–3.4)	0.008
Hypomagnesemia Absent	1.2 (0.9–1.6)	

3.4. Time-to-Event Analysis (Cox Regression)

Kaplan-Meier analysis demonstrated a dose-dependent relationship between K^+ variability and arrhythmia risk. Patients in the highest K^+ variability quartile (median SD=0.50 mmol/L) had a nearly fourfold higher hazard of arrhythmia compared to the lowest quartile (HR=3.9, 95% CI: 2.4–6.4, p<0.001), with a significant trend across quartiles (p-trend <0.001). The median time to readmission was shortest for ventricular tachycardia (10 days, IQR: 5–15) compared to atrial fibrillation (14 days, IQR: 7–21), suggesting that K^+ instability may preferentially trigger life-threatening ventricular arrhythmias in the early post-discharge period. These findings underscore the prognostic value of serial K^+ monitoring during hospitalization, as even subclinical fluctuations portend accelerated arrhythmia onset (Table.4).

Table 4: Time-to-Event Analysis (Cox Regression)

K+ Variability Quartile	Median K+ SD (mmol/L)	Hazard Ratio (HR)	95% CI	p-value
Q1 (Lowest)	0.15	Reference	–	–
Q2	0.25	1.8	1.1–2.9	0.02
Q3	0.35	2.6	1.6–4.3	<0.001
Q4 (Highest)	0.50	3.9	2.4–6.4	<0.001
p-trend	–	–	–	<0.001

3.5. Arrhythmia Type Distribution

Atrial fibrillation (AF) accounted for 50% of readmissions (n=30), followed by ventricular tachycardia (VT, 30%, n=18) and other arrhythmias (20%, n=12). The predominance of AF aligns with its high prevalence in heart failure populations, driven by atrial stretch and fibrosis. However, the shorter median time to VT readmission (10 vs. 14 days for AF) highlights the critical need for early post-discharge surveillance in high-risk patients. Notably, 20% of arrhythmias were classified as "other," including sustained supraventricular tachycardia and bradyarrhythmias, which may reflect autonomic dysregulation or electrolyte-mediated conduction system abnormalities. These data emphasize the diverse arrhythmic manifestations of K^+ instability and the importance of tailored follow-up strategies based on individual risk profiles (Table.5).

Table 5: Arrhythmia Type Distribution

Arrhythmia	Frequency (n=60)	Median Time to Readmission (Days)
Atrial Fibrillation	50% (n=30)	14 (IQR: 7–21)
Ventricular Tachycardia	30% (n=18)	10 (IQR: 5–15)
Other*	20% (n=12)	12 (IQR: 8–18)
*Includes sustained SVT and bradyarrhythmias requiring pacing.		

The results collectively suggest that serum K^+ variability during ADHF hospitalization is a novel, low-cost biomarker for short-term arrhythmia risk, particularly in patients with HFrEF, hypomagnesemia, or high diuretic exposure. The pathophysiological link likely involves K^+-mediated alterations in myocardial repolarization reserve, exacerbated by structural remodeling and neurohormonal activation. Clinically, these findings advocate for: Narrower K^+ targets: Stabilizing K^+ within a tighter range (e.g., 4.0–4.5 mmol/L) during hospitalization. Concomitant Mg^{2+} repletion: Addressing hypomagnesemia to mitigate arrhythmia risk. Risk-stratified follow-up: Prioritizing early ECG monitoring for high-variability patients, especially those with HFrEF. While retrospective designs preclude causal inference, the consistency of associations across multivariable, subgroup, and time-to-event analyses strengthens the hypothesis. Prospective trials testing protocolized K^+ stabilization are warranted to validate these findings.

4. Discussion

This study identifies serum potassium (K^+) variability during hospitalization as a novel, independent predictor of 30-day arrhythmia readmissions in patients with acute decompensated heart failure (ADHF), even after adjusting for absolute K^+ levels, renal function, and diuretic exposure. Our findings extend prior reports linking electrolyte disturbances to adverse outcomes in heart failure (HF) by demonstrating that within-normal K^+ fluctuations—rather than absolute hypo- or hyperkalemia—are clinically significant. This challenges the conventional focus on maintaining K^+ within a broad "normal" range (3.5–5.0 mmol/L) and underscores the need for tighter stabilization, particularly in high-risk subgroups such as those with reduced ejection fraction (HFrEF) or hypomagnesemia. The association between K^+ variability and arrhythmia risk aligns with the electrophysiological principle that myocardial repolarization is exquisitely sensitive to extracellular K^+ concentrations. Even minor fluctuations alter the transmembrane K^+ gradient, increasing dispersion of repolarization and promoting triggered activity via early afterdepolarizations (EADs) and delayed afterdepolarizations (DADs) (Weiss et al., 2017). This mechanism is amplified in HFrEF, where structural remodeling (e.g., fibrosis, connexin-43 downregulation) exacerbates electrical heterogeneity (Nattel et al., 2007). Our observation of a stronger association in HFrEF (aOR=2.2 vs. 1.1 in HFpEF) mirrors findings by Grodzinsky et al. (2020), who reported that HFrEF patients exhibit greater susceptibility to repolarization abnormalities due to ion channel dysfunction. Similarly, the interaction between K^+ variability and hypomagnesemia parallels experimental data showing that Mg^{2+} deficiency impairs Na^+/K^+-ATPase activity, further destabilizing intracellular K^+ concentrations (Viering et al., 2021). These mechanistic insights contextualize our clinical findings and highlight the interplay between electrolyte instability and myocardial substrate in arrhythmogenesis.

Our results contrast with earlier studies that focused solely on absolute K^+ thresholds. For instance, Aldahl et al. (2017) identified hypokalemia (<3.5 mmol/L) as a mortality risk factor in critical care populations but did not explore variability. Similarly, the TOPCAT trial linked hyperkalemia to arrhythmias in HFpEF but excluded patients with normal K^+ levels (Pitt et al., 2014). By contrast, our cohort demonstrated no difference in average K^+ levels between arrhythmia and non-arrhythmia groups (4.2 vs. 4.1 mmol/L, p=0.35), emphasizing that variability—not absolute values—drives risk. This distinction is critical for clinical practice, as current guidelines (Heidenreich et al., 2022) lack recommendations on minimizing K^+ fluctuations. The protective effect of beta-blockers (aOR=0.5)

aligns with their known antiarrhythmic properties, including suppression of sympathetic-driven triggered activity and stabilization of repolarization (Zipes et al., 2006). However, the lower beta-blocker usage in the arrhythmia group (50% vs. 80%) suggests underutilization in high-risk patients, a recurring issue in real-world HF management (Komajda et al., 2017). Similarly, the synergy between high-dose diuretics and K^+ variability (aOR=2.5) underscores the double-edged role of loop diuretics: while essential for decongestion, they exacerbate electrolyte wasting and arrhythmia risk (Ellison & Felker, 2017). These findings advocate for balanced diuretic dosing and routine Mg^{2+} repletion in hypomagnesemic patients, as proposed by Viering et al. (2021).

5. Conclusion

In conclusion, serum K^+ variability during ADHF hospitalization is a clinically actionable biomarker for short-term arrhythmia risk, particularly in HFrEF and hypomagnesemic patients. These findings call for a paradigm shift in electrolyte management—from avoiding extremes to minimizing fluctuations—a strategy that is both feasible and impactful in resource-limited settings. By integrating K^+ stability into routine HF care, clinicians may reduce arrhythmia-related morbidity and improve post-discharge outcomes.

6. Limitations and Future Directions

This study has limitations inherent to retrospective designs, including potential unmeasured confounding (e.g., dietary K^+ intake, outpatient monitoring) and selection bias. The single-center cohort, though representative of real-world ADHF management, requires validation in diverse populations. Additionally, arrhythmia detection relied on readmissions, potentially missing asymptomatic events. Future prospective trials, such as the proposed "K^+-STABLE-HF" trial, should test protocolized K^+ stabilization (e.g., targeting SD <0.3 mmol/L) against standard care, with arrhythmia readmissions as the primary endpoint. Mechanistic studies using patch-clamp electrophysiology could further elucidate how K^+ variability alters ion channel function in human cardiomyocytes.

7. References

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