

RESEARCH ARTICLE

OPEN ACCESS

Emergency Department Serum Electrolyte Patterns in Paroxysmal Atrial Fibrillation

Zahra Hooshanginezhad¹ | Sepehr Nemati² | Mehdi Rezaee³ | Shahin Keshtkar Rajabi⁴ 

¹School of Medicine, Department of Cardiology, Jahrom University of Medical Sciences, Jahrom, Iran | ²BooAli Hospital, Department of Cardiology, Azad University of Medical Sciences, Tehran, Iran | ³Department of Anesthesiology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran | ⁴Firoozabadi Hospital Clinical Research Development Unit (FHCARDU), Department of Internal Medicine, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Correspondence: Shahin Keshtkar Rajabi (dr.keshtkarrajabi@gmail.com)

Received: 7 November 2024 | **Revised:** 28 March 2025 | **Accepted:** 28 March 2025

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Keywords: arrhythmias | atrial | electrolytes | emergency | fibrillation | paroxysmal

ABSTRACT

Background: Little is known about the relationship between circulating electrolyte concentrations and paroxysmal atrial fibrillation in the emergency department. We aimed to characterize circulating electrolyte concentrations in patients with paroxysmal atrial fibrillation compared with those of nonspecific control patients admitted to the emergency department.

Methods: In total, data from 520 individuals with paroxysmal atrial fibrillation and 1,040 randomly selected 1040 patients without atrial fibrillation (1:2 ratio), all admitted to the emergency department (January 2010–December 2015), were analyzed. A classification model was developed using a tree-based machine learning algorithm, and the importance of variables was measured.

Results: Patient age, serum glucose, sodium, potassium, calcium, phosphate, and sex were significantly associated with paroxysmal atrial fibrillation (all $p < 0.001$). For serum magnesium, the difference approached significance ($p = 0.096$). The model had a moderate performance with a 10-fold cross-validation accuracy of 0.728 and a sensitivity, specificity, area under the curve, and likelihood ratio of 0.613, 0.770, 0.692, and 2.67, respectively. Overall, age and glucose were the most important variables followed by serum sodium, potassium, and calcium. Male sex, older age, and a higher serum sodium, calcium, potassium, and magnesium, and a lower serum glucose and phosphate were associated with a higher likelihood of paroxysmal atrial fibrillation in the emergency department.

Conclusion: Serum electrolyte imbalances, particularly in sodium, potassium, and magnesium, are significantly associated with paroxysmal atrial fibrillation in emergency settings. Emergency physicians should monitor and correct these electrolytes to improve early PAF management and potentially prevent adverse outcomes.

1 | Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the general adult population [1]. Patients with AF frequently present to the emergency department (ED) and often require hospitalization, placing a significant burden on clinical facilities [2, 3]. Studies have shown that AF is associated with a higher mortality rate and an increased risk of neurological,

cardiovascular, cognitive, and psychosocial problems [4–8]. Overall, AF has an undesirable effect on the quality of life compared to the general population without AF [9]. Age and sex are independent risk factors of AF [10, 11]. Electrolyte disturbances, altered glucose levels, and endocrine disorders also contribute to the development of AF [12]. There is limited data on the relationship between AF risk and circulating electrolytes, but further studies are needed to validate the findings [13–16].

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2025 The Author(s). *Journal of Clinical Laboratory Analysis* published by Wiley Periodicals LLC

Summary

- Patients with PAF differ from nonspecific controls in blood electrolyte levels.
- Older age and lower sGls were the top important covariates of PAF in the ED.
- Higher sNa, sCa, sK, sMg, and lower sP increase the risk of PAF in the ED.
- Results differ in the ED population compared to the general population.
- Continued research in the emergency setting is warranted.

Characterization of the association of electrolyte concentrations with AF may further suggest the development of prevention or treatment strategies [14]. In general, AF is categorized as first-diagnosed, paroxysmal (terminates spontaneously or with intervention within 7 days of onset), persistent (sustained for ≥ 7 days and/or terminates with cardioversion after ≥ 7 days), long-lasting (duration > 12 months at the time of the decision to adopt a rhythm control strategy) or permanent (accepted by the patient and physician, and no further attempts are made to restore/maintain sinus rhythm will be undertaken) [12]. These subtypes differ in epidemiology, symptoms, management, and prognosis [17]. Most studies of AF were community-based and consisted of a heterogeneous sample of unbalanced AF subtypes [18].

Less is known about the relation between circulating electrolyte concentrations and paroxysmal AF (PAF) in the ED. Nevertheless, because of the paroxysmal character of PAF, it is frequently overlooked, potentially increasing the risk of adverse outcomes such as stroke or heart failure [19]. Studies have confirmed the progressive nature of PAF, suggesting that AF often manifests as paroxysmal and gradually progresses to chronic AF as the outcome [20, 21]. A long-term observational study of patients initially diagnosed with PAF showed a 77% progress to permanent AF [20]. These highlight the importance of evaluating the difference between patients with PAF and controls presenting to the ED.

We conducted this study to characterize circulating electrolyte levels in patients with the main condition of PAF compared with those of other nonspecific control patients without AF admitted to the ED. Our hypothesis was that patients with PAF would differ in blood electrolyte concentrations from other non-AF patients presenting to the ED.

2 | Patients and Methods

2.1 | Design and Data Source

Tazmini et al. conducted a study to investigate the prevalence of electrolyte imbalance in adults presenting to the ED [18]. In a retrospective cohort study, they included all patients ≥ 18 years of age who were presented to the ED for any reason between January 1, 2010, and December 31, 2015, and had blood electrolytes measured. The study was conducted at Diakonhjemmet

Hospital, Oslo, Norway. The hospital has a routine of taking blood samples shortly after the patient arrives at the ED. A total of 62,991 visits from 31,966 patients were recorded in one dataset. In the end, they concluded that patients with electrolyte imbalance had longer hospital stays and were more likely to be readmitted within 30 days of discharge. Diagnosis, monitoring, and treatment of electrolyte imbalance in newly admitted patients were recommended for emergency physicians. Tazmini et al. made their deidentified data publicly available by publishing it as Supporting Information to their article, which is archived in a public data repository [22]. We performed a secondary analysis of the data to provide insights into the associations of circulating electrolyte concentrations with PAF.

2.2 | Ethical Considerations

Our research was in accordance with the Declaration of Helsinki as we did not perform any measurements on the participant. Our study was a secondary analysis of open-access anonymized data. We acknowledged the source of the data and described the efforts of the primary authors. We did not republish raw data but only reported the results of our analysis of existing data. Raw data were licensed under a [Universal \(CC0 1.0\) Public Domain Dedication](#) license and the primary study was approved by a regional committee for medical and health research ethics (Regional Committee for Medical and Health Research Ethics South East).

2.3 | Data Availability

All data and their dictionary are freely deposited in the DRYAD public data repository with a digital object identifier (DOI) of [10.5061/dryad.f3h26j3](#) (publication date: May 08, 2019; Last access date: January 20, 2024) [18, 22].

2.4 | Outcome and Predictors

For each patient, the ICD-10 diagnosis code for the “main condition” and a list of “other conditions” at the time of discharge were recorded under the corresponding headings. Based on the ICD-10 code, patients with the “main condition” of I48.0 code were identified as having PAF. Age (year), sex, serum sodium (sNa; mmol/L), glucose (sGlc; mmol/L), sNa value corrected for sGlc, potassium (sK; mmol/L), calcium (sCa; mmol/L), albumin (sAlb; mmol/L), sCa value corrected for sAlb, phosphate (sP; mmol/L), magnesium (sMg; mmol/L), and plasma free calcium (fCa; mmol/L) were the recorded variables. There were other variables that we did not use in our study, including medical versus surgical department, the length of hospital stay after the date of the ED visit only for patients who died, and the number of days to readmission after discharge only for patients who were readmitted.

2.5 | Data Analysis

The dataset was checked for duplicate rows and missing values. For patients who appeared repeatedly in the dataset, only one

visit was randomly selected. Because of the large imbalance between non-PAF and PAF groups, we randomly selected patients without PAF to obtain a dataset with a 1:2 sample ratio of PAF to non-PAF individuals. The ratio was selected to maintain statistical power while minimizing information loss and ensuring robust interpretable comparisons. This allowed for avoiding overfitting to the majority class. Pairwise correlation analysis was performed not only to identify significant linear relationships but also to guide feature selection by excluding highly correlated variables, thereby minimizing multicollinearity in subsequent multivariable modeling. If the absolute value of the correlation coefficient was greater than 0.5, one variable from each pair was excluded from further analysis. A large number of sP and sMG values were missing from the study dataset. A tree-based machine learning algorithm was used to assess the importance of patient characteristics in discriminating PAF and non-PAF groups. We performed a classification analysis using eXtreme Gradient Boosting (XGBoost) because of its high performance, robustness to the presence of complex relationships between variables, resilience to outliers, and ability to handle unbalanced predictors and missing data [23]. This ensured the analysis of real data without introducing potentially biased imputed values required for logistic regression. In short, XGBoost uses a technique known as “sparse-aware split finding” to effectively calculate the gain in model performance from potential splits while considering missing values as a separate category during the tree-building process. This ensures that the algorithm used the available data as efficiently as possible, thereby reducing the biases that could arise from filling in missing values with artificial estimates. As a result, the performance from each potential split is calculated while accounting for the missing data, ensuring no predictive information is lost. In summary, rather than guessing missing values, the algorithm adjusts its calculations to accommodate them, maintaining the accuracy and reliability of the analysis. We used 10-fold cross-validation to evaluate the performance of the model and measured model performance using standard metrics including accuracy, sensitivity, specificity, positive and negative predictive values, and area under the receiver operating characteristic curve. For the variable importance analysis, both Gain and Cover values were plotted. Gain measures the improvement in predictive accuracy achieved by splitting nodes based on a feature, while Cover quantifies the relative number of times a feature is used for splitting across all trees in the ensemble. Results are presented as

mean (SD) for continuous variables and as absolute numbers (%) for categorical data. Mean values were compared using independent t-tests. For categorical variables, a χ^2 test was used to test for differences between study groups. The significance level was set at two-tailed $\alpha=0.05$. Data analysis and visualization were performed using R software version 4.0.2 for Windows (R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>).

3 | Results

3.1 | Sample

The dataset included 62,991 rows from 31,966 patients. We randomly selected one row for each individual with repeated visits. A total of 520 individuals with the main condition of PAF were identified. We randomly selected 1040 patients without PAF (non-PAF) to provide a dataset with a 1:2 sample ratio of PAF to non-PAF individuals. At the end of the process, the analytic sample included 1560 patients with no repeated data. Figure 1 shows the distribution of age and the sex ratio for both non-PAF and PAF groups. Overall, 18.7% of the data were missing from sGlc (11%), Glc corrected Na (11%), sK (<0.1%), sCa (12%), sAlb (7%), Alb corrected Ca (13%), sP (83%), sMg (79%), and fCa (71%). However, we used the XGBoost algorithm to avoid data imputation.

3.2 | Incorporated Features

We evaluated the set of variables for pairwise linear correlation coefficients of greater than 0.50. There was a high correlation between sNa and Glc-corrected Na (Pearson's $r=0.94$, $p<0.001$), sCa and Alb-corrected Ca ($r=0.71$, $p<0.001$), sCa and fCa ($r=0.59$, $p<0.001$), and sCa and sAlb ($r=0.52$, $p<0.001$). Therefore, fCa and sAlb were excluded as sCa represented both variables, ensuring fewer variables in the model. For the pairs sNa and Glc-corrected Na, and sCa and Alb-corrected Ca, we retained sNa and sCa as they are more commonly reported in clinical settings. These exclusions minimized multicollinearity and adhered to the principle of creating a parsimonious model with the fewest necessary variables while maintaining performance. Figure 2 shows a heatmap of the correlation coefficients. Other

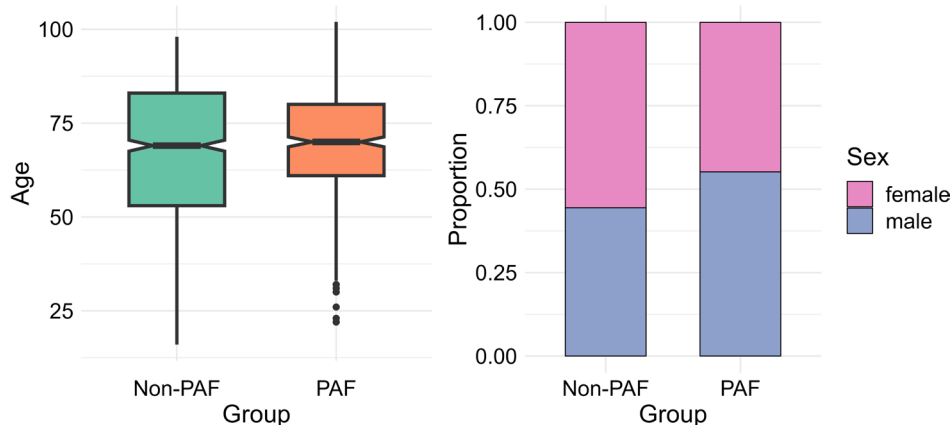


FIGURE 1 | Distributions of age and sex proportions in patients with and without PAF.

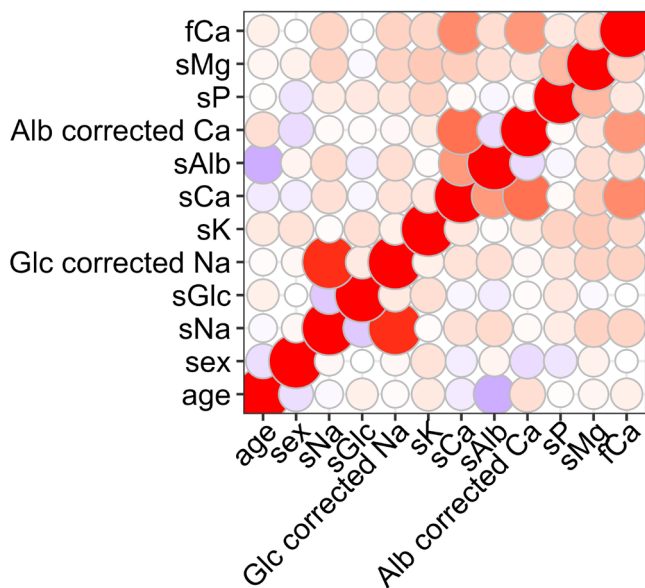


FIGURE 2 | Heatmap of pairwise correlation coefficients between study variables.

variables were included in the next step of the analysis. Table 1 shows the univariate comparison of the two groups of PAF and non-PAF on the selected study variables. All variables, except for sMg, were significantly associated with PAF. For sMg, the *P* value approached significance. Overall, patients with PAF had a higher mean age and higher mean concentrations of sNa, sCa, sK, and sMg, and a lower sGlc and sP than non-PAF patients presenting to the ED. The age range for the non-PAF and PAF groups was 16–98 and 22–102 years, respectively. The male-to-female sex ratio was higher in the PAF group.

3.3 | XGBoost Model

We incorporated the selected features into an XGBoost model and measured its performance using standard metrics in a 10-fold cross-validation. Table 2 shows the performance of the classification model. The model was relatively accurate in classifying PAF versus non-PAF based on patient characteristics. The

kappa coefficient of 0.46 suggested a good agreement between the classifier's predictions and the true labels beyond chance. The classifier was relatively specific in the context of the clinical problem. The positive likelihood ratio of the classifier [sensitivity/(1-specificity)] was 2.67. This means that a positive result increases the probability of PAF. Considering the overall performance of the classifier, we evaluated the importance of the study variables. Figure 3 shows the gain and cover of the included variables. Age and sGlc were the most important covariates of PAF. The next group of importance included sNa, sK, and sCa in decreasing order of importance. Sex, sMg, and sP were of similar and lower importance in their associations with PK.

4 | Discussion

We conducted this study to compare circulating electrolyte concentrations in patients with and without PAF presenting to the ED. Our results showed that patients with PAF differ in blood electrolyte concentrations from nonspecific controls presenting to the ED. We used a well-established supervised machine learning algorithm to develop a model for selecting features associated with PAF. The resulting classifier demonstrated moderate accuracy, sensitivity, and specificity. In particular, the high positive likelihood ratio suggested a high probability of having PAF for a positive result. Despite the large variance inherent in the study problem and the community setting where the data were collected, the study results can be referenced based on the model's performance. The model suggested that patient age, sGlc, sNa, sK, sCa, sex, sMg, and sP were predictors of PAF. Male sex, older age, a higher sNa, sCa, sK, and sMg, and a lower sGlc and sP were associated with a higher likelihood of PAF. Overall, age and sGlc were the top important variables in discriminating patients with and without PAF. Of the serum electrolytes measured, sNa, sK, and sCa were the significant electrolytes in order of importance. These results provide insight into PAF susceptibility in the population of patients presenting to the ED.

To the best of our knowledge, no previous studies have compared serum electrolyte concentrations between groups of patients with and without PAF in the ED. Our results are consistent with previously published research showing electrolyte imbalances

TABLE 1 | The difference between patients with and without PAF. The effect size for sex is the unadjusted odds ratio for the male sex.

Characteristic	Non-PAF (N = 1040)	Missing (%)	PAF (N = 520)	Missing (%)	<i>p</i>
Age (year)	65.74 (20.72)	0.00	69.04 (14.64)	0.00	<0.001*
Male sex	462 (44.4%)	0.00	287 (55.2%)	0.00	<0.001*
sNa (mmol/L)	138.33 (4.07)	0.00	140.21 (3.03)	0.00	<0.001*
sGlc (mmol/L)	7.23 (3.56)	16.06	6.62 (1.82)	1.35	<0.001*
sK (mmol/L)	4.11 (0.50)	0.00	4.25 (0.39)	0.19	<0.001*
sCa (mmol/L)	2.32 (0.15)	18.08	2.35 (0.11)	1.35	<0.001*
sP (mmol/L)	1.11 (0.30)	85.19	1.04 (0.21)	79.42	0.045*
sMg (mmol/L)	0.81 (0.13)	82.60	0.83 (0.07)	72.12	0.096

Abbreviations: sCa, serum calcium; sGlc, serum glucose; sK, serum potassium; sMg, serum magnesium; sNa, serum sodium; sP, serum phosphate.
*Significant at *p* < 0.05.

TABLE 2 | Performance of the XGBoost model in identifying PAF versus non-PAF in patients admitted to the ED. The confusion matrix presents the average percent values of the predicted versus observed classes across all folds of the 10-fold cross-validation.

Model performance (positive class = PAF)		Observed	
		Non-PAF	PAF
Predicted	Non-PAF	56.28	16.86
	PAF	10.38	16.48
Accuracy		0.728	
Kappa coefficient		0.457	
McNemar's test <i>p</i>		0.124	
Sensitivity		0.613	
Specificity		0.770	
Positive predicted value		0.717	
Negative predicted value		0.747	
Area under the curve*		0.692	

Note: Receiver operating characteristic curve.

*Receiver operating characteristic (ROC) curve.

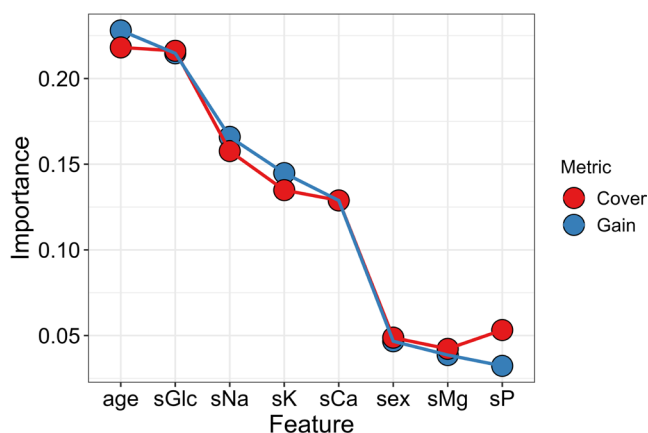


FIGURE 3 | Variable importance using the XGBoost model. Variable importance was assessed using two metrics: Gain and Cover. Gain quantifies the improvement in the model's predictive accuracy when a variable is used to split the data, reflecting its contribution to reducing prediction error. Cover, on the other hand, represents the relative number of observations influenced by a variable across all splits in the model. Briefly, Gain can be thought of as the impact of a variable on improving predictions, while Cover indicates how often the variable is used. sGlc, serum glucose; sNa, serum sodium; sK, serum potassium; sCa, serum calcium; sP, serum phosphate; sMg, serum magnesium.

may contribute to the development of AF. The prevalence of AF in the general population increases with age [24–26]. This association may be explained by the longer period during which risk factors can cause structural changes and less well-defined age-related alterations in cellular electrophysiology [24]. Our research suggested that age has the strongest association with PAF among the study variables. However, it is important to note that all of our patients were referred to the ED. This may have attenuated the relationship between age and PAF in our study, as we

did not compare our patients with PAF to the general population. Studies showed that the incidence of AF is higher in men than in women in all age ranges [24, 26]. We compared controls with the PAF group and not PAF with nonparoxysmal AF. Our study showed that male sex is an independent risk factor for AF. Univariate analysis showed a high unadjusted odds ratio for male sex. However, the importance of sex in our multivariate machine-learning model was not as high as that of age in predicting PAF. Of course, in a study by Al-Makhamreh et al., 47.6% of patients with PAF and 45.2% of patients with nonparoxysmal AF were men [19]. Overall, our research suggested that PAF is more common in men compared to the population of non-AF patients in the ED.

Meanwhile, there is a difference between our results on PAF and what has been reported in the literature regarding the relation between sGlc and AF. Patients with type 2 diabetes, particularly those with poor glycemic control, have been reported to have an increased risk of AF compared to controls from the general population [27, 28]. In our study, sGlc was the second strongest covariate for PAF after age. However, the mean sGlc was lower in patients with PAF. It should be noted that we compared patients with PAF to nonspecific controls presenting to the ED, rather than comparing a heterogeneous sample of patients with AF to the general population. Using a comprehensive multivariable approach, XGBoost evaluated the association of blood glucose with AF by adjusting for other covariates. Moreover, Yang et al. investigated the relationship between fasting glucose levels and AF risk in a large Korean cohort, revealing a U-shaped relationship in patients receiving antidiabetic medication, where both low and high glucose levels increased AF risk [29]. Similar to their findings, our results demonstrate that low glucose levels are associated with AF. In a recent Swedish study of 88,889 patients, including 4948 participants with AF, a model adjusted for a large number of covariates failed to show a significant association between glycemic status and AF [30]. Hypoglycemia has also been reported in patients receiving antiarrhythmic medications, such as beta-blockers or calcium channel blockers [31]. These findings emphasize the need for tailored management of glucose levels to mitigate AF risk in specific patient groups. A recent study by Tascanov et al. explored the relationships between oxidative stress, DNA damage, and PAF, identifying elevated total oxidant status and 8-hydroxy-2'-deoxyguanosine levels as significant predictors of PAF, with total oxidant status ≥ 12.2 showing high sensitivity and specificity [32]. Unlike their focus on systemic oxidative damage, our study highlighted the role of electrolyte imbalances in PAF susceptibility within the ED. Both studies investigated modifiable risk factors. Oxidative stress may play a significant role in influencing atrial remodeling and increasing susceptibility to arrhythmias [32, 33]. Furthermore, its potential synergy with electrolyte disturbances could amplify the risk of arrhythmogenesis, underscoring the need for integrated and multifaceted approaches in future research to better understand and address these interactions. These findings highlight the role of metabolic factors and treatment effects in modulating PAF risk.

In a review study, Rafaqat et al. reported that Ca, Na, and K channels can affect the ion expression of the channel protein, development of fibrosis, transcription of genes, and redistribution of ion channels, which can contribute to the perpetuation

of AF [14]. High sMg was reported to reduce the risk of AF after cardiac surgery, whereas higher sP levels were associated with a higher incidence of AF [14]. In a community study of atherosclerosis, Alonso et al. evaluated the associations of circulating electrolytes with AF and reported that electrolyte concentrations have complex associations with selected arrhythmias [13]. They reported that the top quintiles of sMg, sK, and sP had a lower AF prevalence compared to those in the bottom quintiles. Khan et al. also conducted a study of the Framingham community and suggested that low sMg is moderately associated with AF in individuals without cardiovascular disease [16]. In another community-based cohort study, Lopez et al. found that greater levels of sP were associated with a greater incidence of AF [15]. We found a higher sNa, sCa, sK, and a lower sP or sMg in patients with PAF. However, there are several differences between our study and those reported in the literature. None of the target populations in previously published studies were patients presenting to the ED. The results of some studies can be generalized to patients with a specific disease (e.g., patients with diabetes in Johansson's study [30]). Also, none of the relevant published studies focused exclusively on PAF. Some studies did not provide a detailed report of missing data, and some others did not address the problem of class imbalance in the proportion of patients with AF. Logistic regression has often been used to analyze data without rigorous testing of its statistical preassumptions. Patients with PAF are often referred to the ED. This suggests that nonspecific emergency patients are an appropriate control for comparing patient characteristics. Medical conditions such as hypertension, diabetes mellitus, chronic kidney disease, and congestive heart failure are common in ED patients. These comorbidities can significantly affect electrolyte homeostasis through their effects on renal function and hormone regulation [34]. Patients presenting to the ED often have complex medication regimens, including diuretics, antihypertensives, and antiarrhythmic agents, which can affect electrolyte balance and cardiac electrophysiology. We compared individuals with PAF to nonspecific randomly selected patients in the ED rather than the general population. Our findings suggest the need for continued relevant research in the emergency setting. The observed association between elevated sNa, sCa, sK, sMg, and reduced sP with PAF in the ED may reflect complex electrophysiological interactions at the cellular and tissue levels. Increased extracellular Na can enhance inward depolarizing currents, facilitating triggered activity and abnormal automaticity [35]. Similarly, elevated sCa and sK may contribute to increased intracellular Ca load and early afterdepolarizations, predisposing atrial tissue to fibrillatory conduction [36]. The role of sMg in PAF remains controversial, but higher levels may indicate shifts in intracellular Mg buffering, influencing ion channel kinetics and atrial excitability [37]. Conversely, lower sP levels may reflect altered energy metabolism, impacting ATP-dependent ion transporters and further destabilizing atrial electrophysiology [38]. While our study provides clinical insights, the precise electrophysiological mechanisms underlying these findings necessitate further investigation in basic science studies.

5 | Implications

Our study demonstrates the potential of age- and sex-adjusted circulating electrolyte concentrations to identify PAF in the ED.

Emergency physicians should prioritize the measurement and correction of sNa, sK, and sCa in patients presenting with suspected PAF to reduce the risk of adverse outcomes. Incorporating electrolyte assessment into routine care may improve the early identification of patients at risk for PAF and prevention of PAF progression to persistent AF. This study has several key strengths that contribute to a better understanding of the relationship between serum electrolyte concentrations and PAF. We included a large sample of patients with a wide variety of health conditions. The control patients were randomly selected from a large pool. We used an efficient algorithm to develop the study model with relatively high accuracy given the study question. Finally, the XGBoost technique allowed us to extract knowledge from the existing evidence without imputing missing data. This is particularly important for the large percentages of sMg and sP missing values, where analysis of artificial data could be misleading. The study model can be integrated into decision support systems to automatically identify patients at high risk for PAF in the ED and to signify the need for interventions to reduce the risk of adverse outcomes such as stroke or heart failure.

6 | Limitations

Despite the large sample size, several limitations restrict the generalizability of the findings. In the present dataset, time to death and readmission were recorded only for patients who experienced those events. Therefore, evaluation of the dynamics of PAF incidence and associated risk factors over time, and calculation of hazard ratios were not possible due to the lack of temporal data for all patients. The data were limited to age, sex, primary diagnosis, and serum electrolytes. While comorbidities might further influence PAF risk, the relatively large sample size and random selection of comparison patients from the ED population decrease potential biases due to unmeasured confounders. The primary study was monocentric, which may limit the generalizability of the results. Meanwhile, the outcomes were primarily objective laboratory tests with minimal variability between different nations. With larger sample sizes, it would be possible to evaluate the association of electrolyte concentrations with other types of AF within comorbidity subgroups. Moreover, it would be possible to adjust for the effects of treatment on the development of PAF. Future studies should aim to incorporate detailed information on comorbidities, medication use, and establish cut-off values for electrolyte imbalances. This would allow for a more comprehensive understanding of their direct role in the pathophysiology of PAF, helping to refine risk stratification and therapeutic approaches.

7 | Conclusion

Patients with PAF are commonly referred to the ED, suggesting that nonspecific patients presenting to the ED serve as an appropriate control for comparing patient characteristics between PAF and non-PAF groups. We compared circulating electrolyte concentrations in PAF and non-PAF groups of patients presenting to the ED using a machine learning algorithm. Our results showed significant differences in blood electrolyte levels between patients with PAF and nonspecific controls. The algorithm identified variables including age, sGlc, sNa, sK, sCa,

sex, sMg, and sP as covariates of PAF. Specifically, male sex, advanced age, higher sNa, sCa, sK, and sMg levels, and lower sGlc and sP levels were more associated with PAF. Age and sGlc were the most influential variables in discriminating between PAF and non-PAF patients. Among the serum electrolytes measured, sNa, sK, and sCa were identified as the most significant in predicting PAF risk. These findings provide insight into PAF susceptibility in the ED population and support the integration of electrolyte assessment into routine care to improve AF risk stratification. Further research is warranted to elucidate the underlying mechanisms and refine clinical management strategies for patients with PAF in the ED.

Author Contributions

Z.H. contributed to the literature review, study design, and interpretation of the results. S.N. reviewed the literature and assisted with data analysis. M.R. and S.K.R. conceptualized the study and interpreted the study results. S.K.R. also supervised the study. All the authors participated in drafting. They critically reviewed and approved the final version of this manuscript.

Acknowledgments

We thank Babak Mohammadi (ORCID: 0000-0001-8177-0725) for his assistance in data analysis.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are openly available in DRYAD at <https://doi.org/10.5061/dryad.f3h26j3>.

References

1. M. Zoni-Berisso, F. Lercari, T. Carazza, and S. Domenicucci, "Epidemiology of Atrial Fibrillation: European Perspective," *Clinical Epidemiology* 6 (2014): 213–220, <https://doi.org/10.2147/cep.s47385>.
2. A. J. McDonald, A. J. Pelletier, P. T. Ellinor, and C. A. Camargo, Jr., "Increasing US Emergency Department Visit Rates and Subsequent Hospital Admissions for Atrial Fibrillation From 1993 to 2004," *Annals of Emergency Medicine* 51, no. 1 (2008): 58–65, <https://doi.org/10.1016/j.annemergmed.2007.03.007>.
3. J. Paisey, J. Moss, J. Andrade, et al., "Economic Evaluation of First-Line Cryoballoon Ablation Versus Antiarrhythmic Drug Therapy for the Treatment of Paroxysmal Atrial Fibrillation From an English National Health Service Perspective," *Open Heart* 11, no. 1 (2024): e002423, <https://doi.org/10.1136/openhrt-2023-002423>.
4. V. Ruddox, I. Sandven, J. Munkhaugen, J. Skattebu, T. Edvardsen, and J. E. Otterstad, "Atrial Fibrillation and the Risk for Myocardial Infarction, All-Cause Mortality and Heart Failure: A Systematic Review and Meta-Analysis," *European Journal of Preventive Cardiology* 24, no. 14 (2017): 1555–1566, <https://doi.org/10.1177/2047487317715769>.
5. N. J. Adderley, K. Nirantharakumar, and T. Marshall, "Risk of Stroke and Transient Ischaemic Attack in Patients With a Diagnosis of Resolved Atrial Fibrillation: Retrospective Cohort Studies," *BMJ* 361 (2018): k1717, <https://doi.org/10.1136/bmj.k1717>.
6. A. Nishtala, R. J. Piers, J. J. Himali, et al., "Atrial Fibrillation and Cognitive Decline in the Framingham Heart Study," *Heart Rhythm* 15, no. 2 (2018): 166–172, <https://doi.org/10.1016/j.hrthm.2017.09.036>.

7. K. H. Ladwig, A. Goette, S. Atasoy, and H. Johar, "Psychological Aspects of Atrial Fibrillation: A Systematic Narrative Review: Impact on Incidence, Cognition, Prognosis, and Symptom Perception," *Current Cardiology Reports* 22, no. 11 (2020): 137, <https://doi.org/10.1007/s11886-020-01396-w>.
8. D. Conen, C. U. Chae, R. J. Glynn, et al., "Risk of Death and Cardiovascular Events in Initially Healthy Women With New-Onset Atrial Fibrillation," *Journal of the American Medical Association* 305, no. 20 (2011): 2080–2087, <https://doi.org/10.1001/jama.2011.659>.
9. F. Witassek, A. Springer, L. Adam, et al., "Health-Related Quality of Life in Patients With Atrial Fibrillation: The Role of Symptoms, Comorbidities, and the Type of Atrial Fibrillation," *PLoS One* 14, no. 12 (2019): e0226730, <https://doi.org/10.1371/journal.pone.0226730>.
10. J. G. Andrade, M. W. Deyell, A. Y. K. Lee, and L. Macle, "Sex Differences in Atrial Fibrillation," *Canadian Journal of Cardiology* 34, no. 4 (2018): 429–436, <https://doi.org/10.1016/j.cjca.2017.11.022>.
11. A. Soni, S. Karna, N. Fahey, et al., "Age-and-Sex Stratified Prevalence of Atrial Fibrillation in Rural Western India: Results of SMART-India, a Population-Based Screening Study," *International Journal of Cardiology* 280 (2019): 84–88, <https://doi.org/10.1016/j.ijcard.2018.12.016>.
12. G. Hindricks, T. Potpara, N. Dagres, et al., "2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation Developed in Collaboration With the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the Diagnosis and Management of Atrial Fibrillation of the European Society of Cardiology (ESC) Developed With the Special Contribution of the European Heart Rhythm Association (EHRA) of the ESC," *European Heart Journal* 42, no. 5 (2020): 373–498, <https://doi.org/10.1093/eurheartj/ehaa612>.
13. A. Alonso, M. R. Rooney, L. Y. Chen, et al., "Circulating Electrolytes and the Prevalence of Atrial Fibrillation and Supraventricular Ectopy: The Atherosclerosis Risk in Communities (ARIC) Study," *Nutrition, Metabolism, and Cardiovascular Diseases* 30, no. 7 (2020): 1121–1129, <https://doi.org/10.1016/j.numecd.2020.03.010>.
14. S. Rafaqat, S. Rafaqat, H. Khurshid, and S. Rafaqat, "Electrolyte's Imbalance Role in Atrial Fibrillation: Pharmacological Management," *International Journal of Arrhythmia* 23, no. 1 (2022): 15, <https://doi.org/10.1186/s42444-022-00065-z>.
15. F. L. Lopez, S. K. Agarwal, M. E. Grams, et al., "Relation of Serum Phosphorus Levels to the Incidence of Atrial Fibrillation (From the Atherosclerosis Risk in Communities [ARIC] Study)," *American Journal of Cardiology* 111, no. 6 (2013): 857–862, <https://doi.org/10.1016/j.amjcard.2012.11.045>.
16. A. M. Khan, S. A. Lubitz, L. M. Sullivan, et al., "Low Serum Magnesium and the Development of Atrial Fibrillation in the Community: The Framingham Heart Study," *Circulation* 127, no. 1 (2013): 33–38, <https://doi.org/10.1161/circulationaha.111.082511>.
17. E. D. Almeida, R. B. Guimarães, L. S. Stephan, et al., "Clinical Differences Between Subtypes of Atrial Fibrillation and Flutter: Cross-Sectional Registry of 407 Patients," *Arquivos Brasileiros de Cardiologia* 105, no. 1 (2015): 3–10, <https://doi.org/10.5935/abc.20150049>.
18. K. Tazmini, S. H. Nymo, W. E. Louch, A. H. Ranhoff, and E. Øie, "Electrolyte Imbalances in an Unselected Population in an Emergency Department: A Retrospective Cohort Study," *PLoS One* 14, no. 4 (2019): e0215673, <https://doi.org/10.1371/journal.pone.0215673>.
19. H. Al-Makhamreh, N. Alrabadi, L. Haikal, et al., "Paroxysmal and Non-Paroxysmal Atrial Fibrillation in Middle Eastern Patients: Clinical Features and the Use of Medications. Analysis of the Jordan Atrial Fibrillation (JoFib) Study," *International Journal of Environmental Research and Public Health* 19, no. 10 (2022): 106173, <https://doi.org/10.3390/ijerph19106173>.
20. T. Kato, T. Yamashita, K. Sagara, H. Iinuma, and L. T. Fu, "Progressive Nature of Paroxysmal Atrial Fibrillation. Observations From

- a 14-Year Follow-Up Study,” *Circulation Journal* 68, no. 6 (2004): 568–572, <https://doi.org/10.1253/circj.68.568>.
21. A. J. Shah, M. Hocini, Y. Komatsu, et al., “The Progressive Nature of Atrial Fibrillation: A Rationale for Early Restoration and Maintenance of Sinus Rhythm,” *Journal of Atrial Fibrillation* 6, no. 2 (2013): 849, <https://doi.org/10.4022/jafib.849>.
22. K. Tazmini, S. H. Nymo, W. E. Louch, A. H. Ranhoff, and E. Øie, “Data From: Electrolyte Imbalances in an Unselected Population in an Emergency Department: A Retrospective Cohort Study [Dataset],” *DRYAD* (2019): f3h26j3, <https://doi.org/10.5061/dryad.f3h26j3>.
23. T. Mohammadi, Z. Hooshanginezhad, B. Mohammadi, and S. Dolatshahi, “The Association of Stroke Risk Factors With the Future Thickness of Carotid Atherosclerotic Plaques,” *Neurological Research* 45, no. 9 (2023): 818–826, <https://doi.org/10.1080/01616412.2023.2208484>.
24. K. Wasmer, L. Eckardt, and G. Breithardt, “Predisposing Factors for Atrial Fibrillation in the Elderly,” *Journal of Geriatric Cardiology* 14, no. 3 (2017): 179–184, <https://doi.org/10.11909/j.issn.1671-5411.2017.03.010>.
25. Z. Zathar, A. Karunatileke, A. M. Fawzy, and G. Y. H. Lip, “Atrial Fibrillation in Older People: Concepts and Controversies,” *Frontiers in Medicine* 6 (2019): 175, <https://doi.org/10.3389/fmed.2019.00175>.
26. C. Ohlmeier, R. Mikolajczyk, W. Haverkamp, and E. Garbe, “Incidence, Prevalence, and Antithrombotic Management of Atrial Fibrillation in Elderly Germans,” *Europace* 15, no. 10 (2013): 1436–1444, <https://doi.org/10.1093/europace/eut048>.
27. S. Seyed Ahmadi, A.-M. Svensson, A. Pivodic, A. Rosengren, and M. Lind, “Risk of Atrial Fibrillation in Persons With Type 2 Diabetes and the Excess Risk in Relation to Glycaemic Control and Renal Function: A Swedish Cohort Study,” *Cardiovascular Diabetology* 19, no. 1 (2020): 9, <https://doi.org/10.1186/s12933-019-0983-1>.
28. Y. Sun and D. Hu, “The Link Between Diabetes and Atrial Fibrillation: Cause or Correlation?,” *Journal of Cardiovascular Disease Research* 1, no. 1 (2010): 10–11, <https://doi.org/10.4103/0975-3583.59978>.
29. S. Yang, E. K. Choi, K. D. Han, et al., “Risk of Atrial Fibrillation in Relation to the Time Course of Type 2 Diabetes Mellitus and Fasting Blood Glucose,” *American Journal of Cardiology* 124, no. 12 (2019): 1881–1888, <https://doi.org/10.1016/j.amjcard.2019.09.009>.
30. C. Johansson, L. Örtendahl, M. M. Lind, J. Andersson, L. Johansson, and M. Brunström, “Diabetes, Prediabetes, and Atrial Fibrillation—A Population-Based Cohort Study Based on National and Regional Registers,” *Journal of Internal Medicine* 294, no. 5 (2023): 605–615, <https://doi.org/10.1111/joim.13688>.
31. C. Carnovale, M. Gringeri, V. Battini, et al., “Beta-Blocker-Associated Hypoglycaemia: New Insights From a Real-World Pharmacovigilance Study,” *British Journal of Clinical Pharmacology* 87, no. 8 (2021): 3320–3331, <https://doi.org/10.1111/bcp.14754>.
32. M. B. Tascanov, Z. Tanriverdi, F. Gungoren, et al., “Relationships Between Paroxysmal Atrial Fibrillation, Total Oxidant Status, and DNA Damage,” *Revista Portuguesa de Cardiologia* 40, no. 1 (2021): 5–10, <https://doi.org/10.1016/j.repc.2020.05.011>.
33. Y. Y. Lu, C. C. Cheng, Y. C. Chen, Y. K. Lin, S. A. Chen, and Y. J. Chen, “Electrolyte Disturbances Differentially Regulate Sinoatrial Node and Pulmonary Vein Electrical Activity: A Contribution to Hypokalemia- or Hyponatremia-Induced Atrial Fibrillation,” *Heart Rhythm* 13, no. 3 (2016): 781–788, <https://doi.org/10.1016/j.hrthm.2015.12.005>.
34. T. Mohammadi, S. Tofighi, B. Mohammadi, S. Halimi, and F. Gharebakhshi, “Prognostic Clinical Phenotypes of Patients With Acute De-compensated Heart Failure,” *High Blood Press Cardiovasc Prevention: The Official Journal of the Italian Society of Hypertension* 30, no. 5 (2023): 457–466, <https://doi.org/10.1007/s40292-023-00598-x>.
35. A. G. Kleber and A. L. Wit, “The Interaction Between Na(+) and Ca(2+) Inward Currents in Cardiac Propagation,” *Circulation Research* 127, no. 12 (2020): 1549–1551, <https://doi.org/10.1161/circresaha.120.318316>.
36. J. Heijman, J.-B. Guichard, D. Dobrev, and S. Nattel, “Translational Challenges in Atrial Fibrillation,” *Circulation Research* 122, no. 5 (2018): 752–773, <https://doi.org/10.1161/CIRCRESAHA.117.311081>.
37. B. Ergün, B. Ergan, M. Küçük, et al., “Is Serum Magnesium Level Associated With Atrial Fibrillation in the Mixed Medical/Surgical Intensive Care Unit Setting?,” *Magnesium Research* 35, no. 3 (2022): 96–107, <https://doi.org/10.1684/mrh.2023.0506>.
38. S. Nath, “Phosphorus Chemistry at the Roots of Bioenergetics: Ligand Permutation as the Molecular Basis of the Mechanism of ATP Synthesis/Hydrolysis by F(O)F(1)-ATP Synthase,” *Molecules* 28, no. 22 (2023): 227486, <https://doi.org/10.3390/molecules28227486>.