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Serum Potassium Levels and Atrial Fibrillation Recurrence After Percutaneous Catheter Ablation: A Comprehensive Literature Review

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ABSTRACT

Background: *Atrial Fibrillation (AF) ablation has become the gold standard treatment for symptomatic AF, but recurrence rates remain substantial at 20%-45%. While numerous biomarkers have been investigated as predictors of AF recurrence, the specific role of serum potassium levels and fluctuations during the perioperative period remains underexplored.*

Objective: *To systematically review the literature on the association between serum potassium levels, their variability, and AF recurrence following percutaneous catheter ablation, with particular focus on mechanistic insights, drug effects, procedural differences, and management targets.*

Methods: *A comprehensive search of PubMed and major academic databases was conducted using terms related to atrial fibrillation ablation, serum potassium levels, electrolyte imbalance, and recurrence outcomes.*

Results: *Limited but emerging evidence suggests that serum potassium levels may influence AF recurrence after ablation through multiple mechanisms involving ion channel function, cellular electrophysiology, and autonomic modulation. Mineralocorticoid receptor antagonists significantly affect potassium homeostasis and may influence AF outcomes. Different ablation techniques have varying impacts on perioperative electrolyte changes. Current evidence is insufficient to establish specific potassium management targets for post-ablation care.*

Conclusion: *While preliminary evidence suggests potential relationships between serum potassium levels and AF recurrence, dedicated large-scale prospective studies are needed to establish definitive associations, optimal management protocols, and evidence-based guidelines.*

Keywords: Atrial fibrillation, Serum potassium, Catheter ablation

INTRODUCTION

Atrial Fibrillation (AF) affects millions of patients worldwide and represents the most common sustained cardiac arrhythmia in clinical practice [1,2]. Catheter ablation, particularly Pulmonary Vein Isolation (PVI), has emerged as the most effective therapeutic intervention for maintaining sinus rhythm in patients with symptomatic AF [3]. However, despite significant advances in ablation techniques and technologies, recurrence rates remain substantial, ranging from 20% to 45% in most series, representing a significant clinical challenge [4-6].

The complex pathophysiology underlying AF recurrence involves multiple factors, including structural remodeling, inflammatory processes, and electrophysiological changes [7-9]. Numerous biomarkers have been investigated as predictors of post-ablation outcomes, with established associations demonstrated for natriuretic peptides (ANP, BNP, NT-pro-BNP), inflammatory markers (C-reactive protein, IL-6) and markers of atrial remodelling [10-16].

Serum potassium plays a fundamental role in cardiac electrophysiology through its effects on membrane potential, cellular excitability, and ion channel function [16-18]. Alterations in potassium homeostasis can significantly influence arrhythmogenesis through effects on repolarization, refractoriness, and conduction properties [19-21]. Despite this mechanistic rationale, the specific relationship between serum potassium levels and AF recurrence after catheter ablation has received limited systematic investigation.

MATERIALS AND METHODS

A systematic literature search was conducted using PubMed, EMBASE, Google Scholar, and major Japanese medical databases, including J-STAGE. Search terms included combinations of "atrial fibrillation," "catheter ablation," "serum potassium," "hypokalemia," "hyperkalemia," "electrolyte imbalance," "recurrence," "mineralocorticoid receptor antagonists," "ablation techniques," and "outcomes." The search encompassed publications from inception through August 2025, with a particular focus on Japanese studies and Asian populations

RESULTS, LITERATURE ANALYSIS AND DISCUSSION

Limited direct evidence on potassium-recurrence relationships

The systematic review revealed a notable paucity of studies specifically investigating the relationship between serum potassium levels and AF recurrence after catheter ablation. A comprehensive meta-analysis by Jiang, et al., examining pre-ablation blood markers associated with AF recurrence, analyzed 36 studies covering 11 different biomarkers, including natriuretic peptides, inflammatory markers, lipid parameters, and fibrosis markers; however, it notably did not include serum potassium levels in its analysis [12].

Recent preliminary evidence has begun to address this knowledge gap. A notable study by Yang, et al., specifically investigated the association between serum potassium level and AF recurrence after catheter ablation, demonstrating the relationship between potassium and recurrence [22].

Mechanistic understanding: Molecular and cellular basis

The molecular basis of AF involves multiple types of potassium channels that are crucial for maintaining normal cardiac electrophysiology [8]. Understanding these mechanisms is crucial for comprehending how serum potassium alterations may impact post-ablation outcomes. Major potassium channel types in atrial tissue are as follows:

1. Voltage-Gated Potassium Channels

1. IKr (Rapid Delayed Rectifier): Encoded by KCNH2 (hERG), crucial for late repolarization
2. IKs (Slow Delayed Rectifier): Encoded by KCNQ1, important for action potential duration control
3. IK1 (Inward Rectifier): Encoded by KCNJ2, maintains resting membrane potential
4. Ito (Transient Outward): Encoded by KCND3, controls the early repolarization phase

2. ATP-Sensitive Potassium Channels (KATP)

1. Encoded by KCNJ11 and ABCC9
2. Activated during metabolic stress and ischemia
3. Link cellular metabolism to electrical activity

3. Acetylcholine-Activated Potassium Channels (IKACh)

1. Encoded by KCNJ3 and KCNJ5
2. Mediate parasympathetic effects on atrial electrophysiology
3. Particularly relevant in vagally-mediated AF

Hypokalemia-induced changes

Hypokalemia hyperpolarizes the resting membrane potential, increasing the driving force for sodium influx during depolarization [23]. This can enhance automaticity in atrial tissue, particularly in areas of slow conduction such as the pulmonary vein-left atrial junction. Low extracellular potassium reduces IK1 current, prolonging action potential duration and creating dispersion of repolarization [23,24]. This heterogeneity in repolarization provides the substrate for reentrant arrhythmias. Hypokalemia also affects intracellular calcium homeostasis through alterations in sodium-potassium pump activity, which can potentially increase delayed afterdepolarizations and triggered activity [25].

Hyperkalemia-induced changes

Elevated potassium levels depolarize resting membrane potential, reducing sodium channel availability and slowing conduction velocity [23]. This can create areas of unidirectional block facilitating reentry. Furthermore, hyperkalemia shortens action potential duration by enhancing outward potassium currents, potentially destabilizing electrical activity in the post-ablation atrium.

Molecular remodeling in AF and post-ablation healing

AF-induced electrical remodeling involves downregulation of L-type calcium channels and alterations in potassium channel expression [26-29]. These changes persist into the post-ablation period and may be influenced by prevailing electrolyte conditions:

1. IKur Upregulation: Increased ultra-rapid delayed rectifier current contributes to action potential shortening
2. IK1 Enhancement: Increased inward rectifier current stabilizes shortened action potentials
3. ICa, L Reduction: Decreased calcium current reduces action potential duration and contractility

The post-ablation healing process involves the activation of fibroblasts and the deposition of collagen. Potassium levels may influence this process through effects on fibroblast proliferation and differentiation, modulation of inflammatory cytokine release, and alterations in growth factor signaling pathways.

Drug effects on potassium homeostasis and AF outcomes

Spironolactone competitively inhibits aldosterone binding to mineralocorticoid receptors in the distal nephron, reducing sodium reabsorption and potassium excretion [30]. This leads to potassium retention and potential hyperkalemia. A meta-analysis by Liu, et al., demonstrated that spironolactone significantly reduced AF recurrence (OR 0.58, 95% CI 0.37-0.90, p=0.01) [31]. The anti-AF effects appear to involve multiple mechanisms: spironolactone affects multiple ion currents, including the reduction of L-type calcium current and the enhancement of transient outward potassium current [32]. Furthermore, spironolactone induces a reduction in atrial fibrosis by inhibiting collagen synthesis and myofibroblast differentiation, as well as decreasing the expression of inflammatory markers and reducing oxidative stress [33]. Spironolactone therapy typically increases serum potassium by 0.5-1.0 mEq/L [34]. In the post-ablation setting, this effect must be carefully monitored to prevent hyperkalemia while potentially providing anti-arrhythmic benefits.

Eplerenone exhibits greater selectivity for mineralocorticoid receptors compared to spironolactone, resulting in reduced anti-androgenic side effects [35,36]. A meta-analysis showed that eplerenone specifically reduced AF recurrence (OR 0.48, 95% CI 0.26-0.89, p=0.02), with effects potentially mediated through the reduction of atrial effective refractory period heterogeneity, a decrease in inward rectifier potassium current, and anti-remodeling effects on atrial structure [31].

Finerenone (next-generation non-steroidal Mineralocorticoid Receptor Antagonist (MRA)) demonstrates tissue selectivity and may have different effects on sodium and potassium balance compared to steroidal MRAs [37,38]. Early studies suggest a reduced risk of hyperkalemia while maintaining cardiovascular benefits. While data specific to AF are limited, finerenone's favorable potassium profile may make it an attractive option for post-ablation management, although this requires further investigation.

Both ACE inhibitors and Angiotensin Receptor Blockers (ARBs) can increase serum potassium levels by reducing aldosterone production [39,40]. In the post-ablation setting, these effects may interact with the arrhythmogenic potential of potassium alterations.

Beta-blockers can influence potassium homeostasis through effects on renin-angiotensin-aldosterone system activity, cellular potassium uptake mechanisms, and stress-induced catecholamine effects on potassium distribution [41,42]. The combination of beta-blockade with altered potassium levels in the post-ablation period may affect heart rate variability, autonomic balance, exercise tolerance, potassium shifts during physical activity, and long-term electrical remodeling processes [43,44].

Ablation technique-specific effects on electrolyte balance

Studies by Chopra, et al., demonstrated that Radio Frequency (RF) ablation using high-volume irrigated catheters causes significant perioperative electrolyte disturbances [45]. ThermoCool catheters (high-volume irrigation) causes significant potassium reduction (4.4 ± 0.42 *vs* 4.0 ± 0.32 mmol/L; p<0.001). However, Surround Flow catheters (lower-volume irrigation) do not induce significant potassium change (4.4 ± 0.3 vs 4.2 ± 0.4 mmol/L; p=0.16) [45]. Large saline volumes stimulate potassium secretion in the distal nephron. Rapid volume expansion dilutes existing serum potassium, and compensatory diuresis further depletes potassium stores [46]. Modern RF ablation with contact force sensing may reduce the need for high-volume irrigation by delivering energy more efficiently. This could potentially minimize electrolyte disturbances while maintaining lesion quality [47].

Cryoballoon procedures typically involve less irrigant volume compared to RF ablation, potentially resulting in reduced perioperative volume expansion, less dramatic potassium shifts, and different inflammatory response patterns [48,49]. Cryothermal injury may have distinct effects on cellular potassium handling (different patterns of cellular membrane disruption [50], altered inflammatory cascade activation and potentially different healing responses affecting long-term electrolyte sensitivity) compared to RF ablation [51].

Pulsed Field Ablation (PFA) represents a newer ablation modality with potentially different effects on cellular and systemic electrolyte balance [52]. As the theoretical advantages, selective tissue targeting may reduce collateral electrolyte disturbances, and non-thermal mechanism may preserve cellular membrane integrity. Furthermore, PFA reduced procedure-related fluid administration [53]. However, current evidence on PFA-specific electrolyte effects is limited, representing an important area for future investigation.

Patients undergoing repeat ablation procedures may experience cumulative effects on potassium homeostasis due to repeated volume expansion and diuresis cycles, progressive atrial remodeling that affects autonomic innervation, and adjustments in medication between procedures [4].

Post-ablation potassium management: Targets and monitoring

Current post-ablation care protocols vary significantly across centers regarding electrolyte management. There are no established potassium target ranges specific to post-ablation care with variable timing and frequency of electrolyte monitoring. Furthermore, we have inconsistent approaches to potassium supplementation.

Major society guidelines (AHA/ACC/HRS, ESC/EHRA) provide limited specific guidance on post-ablation electrolyte management, typically recommending [54-56]:

1. Correction of electrolyte abnormalities without specific targets
2. Monitoring "as clinically indicated" without defined protocols
3. General recommendations for maintaining "normal" potassium levels (3.5-5.0 mEq/L)

High-risk patients (previous electrolyte-related arrhythmias, chronic kidney disease or heart failure, concurrent MRA or ACE inhibitor/ARB therapy, or multiple comorbidities affecting potassium homeostasis) need enhanced monitoring; standard-risk patients (normal baseline renal function, no significant comorbidities, or standard medication regimens) need routine monitoring [57].

At the immediate post-ablation period (0-24 hours), baseline potassium measurements are taken at pre-procedure and 6–12-hour post-procedure assessments [58]. The target range is 4.0-4.5 mEq/L (slightly high-normal), and serum potassium values <3.5 or >5.0 mEq/L are immediately corrected. As a short-term follow-up (1-4 weeks), weekly potassium monitoring is performed for high-risk patients and bi-weekly monitoring for standard-risk patients. Target range is 4.0-4.5 mEq/L. As a long-term management (1-12 months), monthly monitoring during the blanking period (first 3 months). Is done with target range 3.8-4.8 mEq/L (allowing broader range with stability).

Integration with arrhythmia monitoring

Future research should investigate correlations between the potassium levels at the time of documented arrhythmia recurrence, patterns of potassium variability, and arrhythmia burden. Furthermore, optimal potassium levels for individual patients, based on their recurrence history, should be discussed and tailored accordingly. Modern monitoring approaches may include the integration of electrolyte data with implantable cardiac monitors, the development of predictive algorithms that incorporate potassium trends, and patient-specific targeting based on individual electrophysiological profiles.

Japanese research contributions and Asian population studies

A recent multicenter Japanese study (Kansai Plus AF Registry) investigated AF ablation outcomes in hemodialysis patients, highlighting the importance of electrolyte management in this high-risk population [59]. Key Findings are as follows: 1) Electrolyte shifts after dialysis contribute to AF development and poor ablation outcomes; 2) Dynamic changes in intravascular volume and electrolytes increase the likelihood of atrial premature contractions triggering AF; and 3) Hemodialysis patients demonstrated higher AF recurrence rates compared to non-dialysis patients. The study identified dramatic changes in plasma composition during dialysis, sympathetic nervous system stimulation from volume changes, and enhanced susceptibility to triggered arrhythmias several mechanisms by which dialysis-related electrolyte changes promote AF. These findings suggested that we need specialized electrolyte monitoring protocols, potential timing of ablation procedures, and enhanced post-procedural monitoring in dialysis patients.

Another large Japanese multicenter study (KiCS-AF Multicenter Cohort Study) examined catheter ablation outcomes across a broad spectrum of heart failure patients [60]. Relevant Findings demonstrated that successful ablation outcomes were achieved with comprehensive medical management, including electrolyte balance, in both preserved and reduced ejection fraction heart failure. This study's findings suggest that heart failure patients may require different electrolyte management strategies and that integrated care approaches, including electrolyte monitoring, improve results.

As future directions for Japanese research, we need to investigate the genetic factors affecting potassium homeostasis in Asian populations, study dietary potassium intake patterns and AF outcomes, and evaluate the effects of traditional Japanese medications on electrolyte balance. Furthermore, the development of artificial intelligence-assisted electrolyte monitoring systems, integration with Japan's digital health infrastructure, and personalized medicine approaches based on genetic and metabolic profiling will be necessary.

Gaps in current literature and future research directions

There are many critical knowledge gaps in this field. As mechanistic understanding, limited data on optimal potassium levels for individual patients, insufficient understanding of potassium variability effects, and lack of real-time monitoring correlation with arrhythmia events are still not clarified. As clinical applications, there are no validated risk stratification tools incorporating potassium levels and cost-effectiveness analyses for enhanced monitoring protocols. We have limited data on intervention trials for targeted potassium management.

Considering these unsolved problems, large-scale prospective cohort studies with multi-centre international collaboration, standardized potassium measurement protocols, long-term follow-up with continuous arrhythmia monitoring, and adequate statistical power for subgroup analyses are needed. In this future study, recommended primary endpoints are time to first AF recurrence after a blanking period, arrhythmia burden on continuous monitoring, quality of life measures, and healthcare utilization costs.

Moreover, as randomized controlled trials, we need the intervention or mechanistic studies:

1. Targeted potassium management trial: Randomized comparison of intensive *vs.* standard potassium monitoring and management.
2. MRA Therapy Trial: evaluation of prophylactic mineralocorticoid receptor antagonist therapy post-ablation.
3. Ablation technique comparison: Direct comparison of electrolyte effects across different ablation modalities.
4. Ion channel function studies: Investigation of potassium level effects on specific ion channel function in post-ablation atrial tissue.
5. Biomarker integration studies: Evaluation of potassium levels in combination with established predictive biomarkers.
6. Genetic association studies: Investigation of genetic variants affecting potassium homeostasis and AF recurrence risk.

CONCLUSION

This comprehensive literature review reveals that, while the mechanistic rationale for the relationships between serum potassium levels and AF recurrence after catheter ablation is compelling, current evidence provides only limited direct clinical data to support these associations. Several important findings emerge:

1. Strong theoretical and experimental evidence supports the role of potassium homeostasis in cardiac electrophysiology and arrhythmogenesis, with multiple ion channel types and cellular mechanisms contributing to this process.
2. Mineralocorticoid receptor antagonists, particularly spironolactone and eplerenone, demonstrate both anti-AF effects and significant impacts on potassium homeostasis, suggesting potential therapeutic targets.
3. Different ablation modalities appear to have varying effects on perioperative electrolyte changes, with RF ablation using high-volume irrigation causing more significant potassium depletion.
4. Current clinical practice lacks standardized protocols for post-ablation potassium monitoring and management, representing an opportunity for improvement.
5. Studies from Japan, particularly in specialized populations such as hemodialysis patients, provide valuable insights into electrolyte management in AF ablation.

The evolving understanding of electrolyte roles in AF pathophysiology, combined with improving ablation outcomes and longer follow-up periods, creates an opportune time to investigate these relationships systematically. Priority areas include large-scale prospective cohort studies designed specifically to investigate potassium levels as predictors of AF recurrence, randomized controlled trials examining targeted potassium management strategies, mechanistic studies investigating ion channel function and cellular electrophysiology, technology development for real-time monitoring and personalized management, and international collaborative efforts to establish evidence-based guidelines.

Until definitive evidence becomes available, clinicians should consider enhanced awareness of potassium levels during the perioperative period, individualized monitoring protocols based on patient risk factors, careful management of medications affecting potassium homeostasis, and integration of electrolyte management with overall post-ablation care.

The potential for improved AF ablation outcomes through optimized electrolyte management represents an important frontier in cardiac electrophysiology, warranting continued investigation and clinical attention.

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