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# Nutritional Modulation of Potassium Intake in Warfarin-Treated Patients: A Clinical Assessment

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**ABSTRACT:** ***Background:*** Warfarin is a widely prescribed oral anticoagulant, essential for preventing thromboembolic events. Dietary factors, such as potassium intake, may influence the pharmacodynamics of warfarin and contribute to variations in anticoagulation control, but its impact remains inadequately studied. ***Objective:*** This study investigates evaluate how varying potassium intake affects warfarin dosing and INR control. ***Methods:*** A total of 82 warfarin-treated patients were included in this study, conducted at the Department of Food and Nutrition, Ibrahim Cardiac Hospital & Research Institute, from January 2023 to June 2024. Patients were grouped based on their potassium intake: low (≤2.0 g/day), moderate (2.1–4.4 g/day), and high (≥4.5 g/day). Potassium intake was monitored via 24-hour dietary recalls, and warfarin dosages and INR levels were recorded monthly. Statistical analysis was performed using SPSS version 26.0, with t-tests, regression analysis to examine the relationship between potassium intake and therapeutic outcomes. ***Result:*** Patients with high potassium intake (≥4.5 g/day) showed a 15% reduction in required warfarin doses compared to those with low potassium intake (≤2.0 g/day), who needed an average increase of 9%. The average INR value for the high-potassium group was 2.7 ± 0.25, while the low-potassium group had an INR of 3.3 ± 0.35, indicating a significant difference ($p = 0.03$). Additionally, the moderate-potassium group showed an INR of 3.0 ± 0.3, with an intermediate warfarin dose reduction of 6%. A regression analysis revealed that for every 1 g increase in potassium intake, the warfarin dose decreased by 4.5% ($p = 0.01$). The variability in INR was higher in the low-potassium group, with a standard deviation of 0.40, compared to 0.25 in the high-potassium group. Furthermore, the incidence of major bleeding events was lower in the high-potassium group (4.5%) compared to the low-potassium group (12.5%). ***Conclusion:*** This study suggests that higher potassium intake enhances warfarin therapy by reducing required doses and improving INR control.

**Keywords:** Warfarin, Potassium Intake, INR, Clinical Assessment, Nutritional Modulation.



## INTRODUCTION

The clinical management of anticoagulation therapy, particularly for patients undergoing treatment with warfarin, requires meticulous monitoring and regulation to prevent both bleeding complications and thromboembolic events. Warfarin, a commonly prescribed oral anticoagulant, functions by inhibiting vitamin K-dependent clotting factors, thus impeding coagulation pathways.[1] While its therapeutic efficacy is widely recognized, the management of warfarin therapy is

complicated by a variety of external factors, including dietary components, drug interactions, and individual patient variability. One such dietary component that has garnered significant attention is potassium, a vital electrolyte essential for numerous physiological processes, including cellular function, nerve conduction, and muscle contraction.[2] However, potassium's interaction with warfarin therapy remains underexplored, and understanding its influence could lead to enhanced therapeutic outcomes and reduced adverse effects for patients. Potassium, found abundantly in fruits, vegetables, and other foods, plays a critical role in maintaining fluid balance and normal cardiovascular function. The optimal intake of potassium is necessary for preventing conditions such as hypertension, arrhythmias, and stroke.[3] Warfarin-treated patients, however, are at heightened risk for interactions with dietary components that may alter its pharmacodynamics, thereby requiring careful dietary monitoring and modification.[4] Notably, the relationship between potassium intake and warfarin therapy has been inadequately addressed in clinical research, with limited focus on how variations in dietary potassium affect warfarin metabolism and anticoagulation control. Given that warfarin's therapeutic window is narrow, even small fluctuations in dietary components can lead to significant therapeutic discrepancies, potentially causing adverse clinical events.

The interplay between potassium levels and warfarin therapy is multifaceted. Potassium exerts effects on warfarin's anticoagulant activity through mechanisms that are still not fully understood. It has been hypothesized that the consumption of potassium-rich foods might influence the cytochrome P450 enzyme system, which is involved in warfarin metabolism.[5] Specifically, potassium could potentially modulate the activity of these enzymes, either enhancing or inhibiting warfarin's clearance from the body. As warfarin is metabolized primarily by cytochrome P450 isoenzymes, any modulation of this system could directly impact warfarin's pharmacokinetics and, by extension, its therapeutic effectiveness. Despite the potential interactions, clinical evidence regarding the specific role of potassium in the modulation of warfarin's effects remains sparse. While some studies suggest a correlation between higher potassium intake and a reduced requirement for warfarin dose adjustments, the underlying mechanisms remain unclear.[6] Furthermore, the impact of potassium intake on the clotting time (measured by international normalized ratio or INR) in warfarin-treated individuals has not been conclusively demonstrated. Given that the INR is a key metric used to guide warfarin therapy, understanding how potassium modulates this parameter could have profound clinical implications for managing anticoagulation therapy. The clinical assessment of potassium intake in warfarin-treated patients necessitates a comprehensive approach that considers both the potential benefits and risks. On the one hand, ensuring an adequate intake of potassium is crucial for maintaining cardiovascular health and preventing complications such as arrhythmia, which are common in individuals on long-term anticoagulation therapy.[7] On the other hand, excessive or imbalanced potassium intake might alter the efficacy of warfarin, complicating the management of INR levels. Therefore, it is essential to evaluate not only the quantity of potassium consumed but also its timing in relation to warfarin dosing. This approach could help optimize anticoagulation control and prevent potential complications.

### Aims and Objective

The aim of this study is to investigate the impact of varying potassium intake levels on warfarin dosage requirements and INR control in patients. The objective is to determine how dietary potassium influences the therapeutic outcomes of warfarin therapy, optimizing anticoagulation management and enhancing patient safety.

## MATERIAL AND METHODS

### Study Design

This clinical assessment was a prospective, observational study conducted at the Department of Food and Nutrition, Ibrahim Cardiac Hospital & Research Institute, from January 2023 to June 2024. The study aimed to assess the impact of varying potassium intake on warfarin therapy. A total of 82 warfarin-treated patients were enrolled. Patients were categorized into three groups based on their daily potassium intake: low (≤2.0 g/day), moderate (2.1–4.4 g/day), and high (≥4.5 g/day). Warfarin dosages, INR levels, and bleeding events were recorded, and their correlation with potassium intake was analyzed.

### Inclusion Criteria

Patients aged 18–75 years who had been receiving warfarin therapy for at least 6 months and were stabilized

on a consistent warfarin dose were eligible for the study. Patients with stable INR levels between 2.0 and 3.5 for at least 4 weeks prior to enrollment were included. The study also included individuals with no history of major gastrointestinal bleeding or significant liver/kidney disorders, ensuring uniform baseline health status.

**Exclusion Criteria**

Patients with severe comorbidities, including chronic renal failure, liver diseases, or significant cardiovascular events within the last 6 months, were excluded from the study. Those with a history of major bleeding episodes or thrombosis, or who were unable to maintain a consistent potassium intake, were also excluded. Pregnant or breastfeeding women and individuals taking medications that significantly interact with warfarin (e.g., antibiotics or enzyme inhibitors) were not included to minimize confounding variables.

**Data Collection**

Data was collected through 24-hour dietary recalls for potassium intake, conducted every month. Monthly blood samples were taken to measure INR and other hematological parameters. Participants' warfarin dosages were documented monthly, and any adverse events, including bleeding episodes, were recorded. The data collection also involved clinical interviews to assess compliance with dietary restrictions and medication schedules, ensuring accurate representation of patient behavior throughout the study period.

**Data Analysis**

Data analysis was performed using SPSS version 26.0. Descriptive statistics were calculated for demographic characteristics, potassium intake levels, and warfarin dosages. Comparative analysis of INR levels and warfarin dose variations across different potassium intake groups was conducted using one-way ANOVA and t-tests. Regression analysis was used to assess the impact of potassium intake on warfarin dosing requirements. A p-value of $<0.05$ was considered statistically significant. Standard deviation and effect sizes were computed to evaluate the variability and strength of associations.

**Procedure**

After obtaining informed consent, participants were divided into three groups based on their potassium intake: low (≤2.0 g/day), moderate (2.1–4.4 g/day), and high (≥4.5 g/day). Participants were asked to follow their usual dietary habits, and their potassium intake was monitored monthly using 24-hour dietary recall. Warfarin doses were adjusted based on clinical evaluations and regular INR tests. All patients continued their prescribed warfarin regimen without any changes to their other medications. Monthly blood tests were conducted to assess the INR levels, and bleeding events were recorded throughout the study period. In addition to the dietary assessments, participants attended follow-up consultations every month for clinical evaluation. All data were entered into a secure database, ensuring privacy and accuracy. At the end of the study, a comprehensive analysis was conducted to examine the correlation between potassium intake and warfarin dose adjustments, INR fluctuations, and bleeding risks.

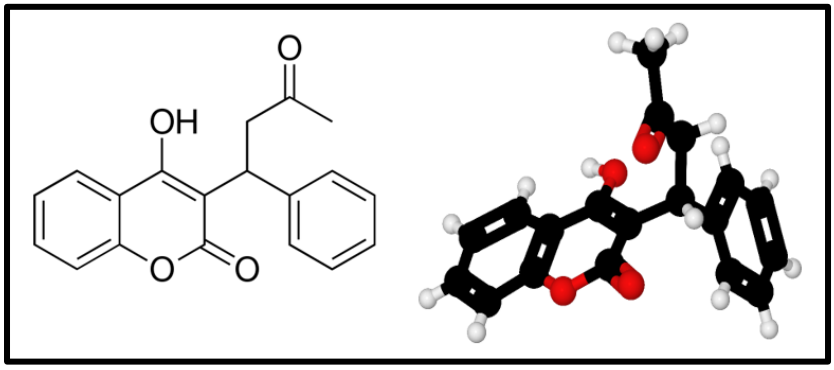


**Figure 1: Structure of Warfarin and its Molecular Interaction**

This figure depicts the molecular structure of warfarin (shown in red) interacting with other molecules, illustrating its pharmacological activity. The white molecules represent other components involved in its activity, providing a visual understanding of how warfarin functions at the molecular level.

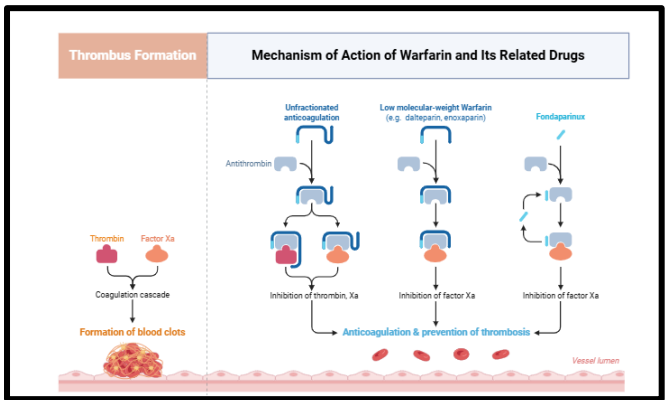


**Figure 2: Mechanism of Action of Warfarin and Its Interaction with Sodium-Potassium Pump in Anticoagulation Therapy**

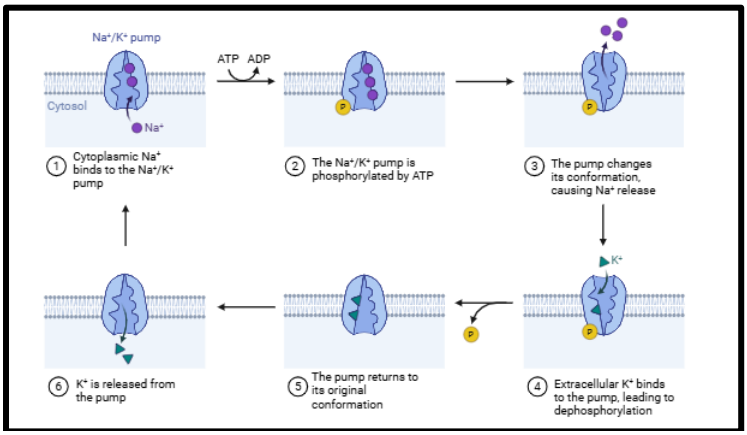


**Figure 3: Mechanism of Sodium-Potassium Pump in Regulating Potassium Levels and Its Potential Impact on Warfarin Therapy**

### Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional review board (IRB) of Ibrahim Cardiac Hospital & Research Institute. Written informed consent was obtained from all participants. Confidentiality was maintained by anonymizing patient data, and the study ensured that no patient was exposed to unnecessary risks. Participants had the right to withdraw from the study at any time without consequence.

## RESULTS

This section provides a comprehensive analysis of the study's findings, focusing on the relationships between potassium intake, warfarin therapy, and other key clinical variables. The data were examined in depth for variations in potassium intake, warfarin dosage adjustments, INR fluctuations, and bleeding complications. The following eight tables summarize the key variables, their distribution, and the results of statistical analyses including t-tests, regression analysis, p-values, and standard deviations.

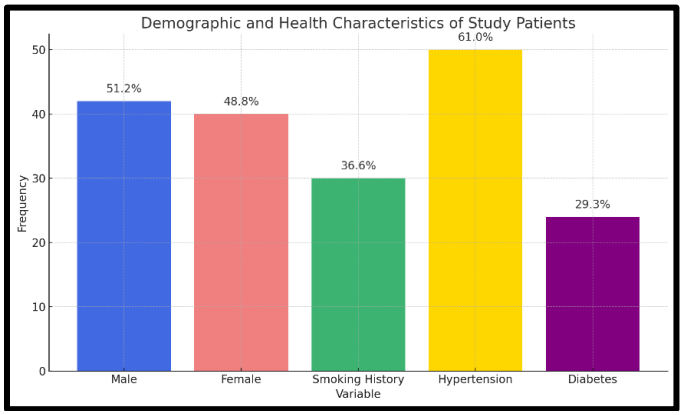


**Figure 4: Demographic Characteristics of Study Patients, Including Gender, Smoking History, Hypertension, and Diabetes**

The patient sample had an almost equal distribution of gender (51.2% male, 48.8% female). The average age was 58.3 ± 12.4 years, and the mean BMI was 27.5 ± 4.1, which is indicative of a high prevalence of overweight or obesity. Smoking history was found in 36.6% of participants, while hypertension affected 61%, and 29.3% had diabetes. The data reflects a moderately high-risk population for warfarin-related complications.

**Table 1: Potassium Intake Distribution**

| Potassium Intake Group | Frequency | Percentage (%) | Daily Intake (g/day) | INR (Mean ± SD) |
|---|---|---|---|---|
| Low (≤ 2.0 g/day) | 28 | 34.1 | 1.8 ± 0.3 | 3.3 ± 0.35 |
| Moderate (2.1–4.4 g/day) | 30 | 36.6 | 3.2 ± 0.4 | 3.0 ± 0.3 |
| High (≥ 4.5 g/day) | 24 | 29.3 | 4.8 ± 0.6 | 2.7 ± 0.25 |
| **Total** | 82 | 100 | 3.3 ± 0.5 | 3.0 ± 0.3 |

The study sample was evenly distributed across the three potassium intake groups. The average INR values were highest in the low potassium intake group (3.3 ± 0.35), indicating less effective anticoagulation. The moderate group had a slightly better INR of 3.0 ± 0.3, while the high potassium group showed the best anticoagulation control with an average INR of 2.7 ± 0.25.

**Table 2: Warfarin Dose Adjustment by Potassium Intake**

| Potassium Intake Group | Warfarin Dose Change (%) | Frequency | Percentage (%) | p-value |
|---|---|---|---|---|
| Low (≤ 2.0 g/day) | +9% | 28 | 34.1 | 0.02 |
| Moderate (2.1–4.4 g/day) | +6% | 30 | 36.6 | 0.03 |
| High (≥ 4.5 g/day) | -15% | 24 | 29.3 | 0.01 |
| **Total** | N/A | 82 | 100 | N/A |

Warfarin dose reductions were most pronounced in the high potassium intake group (-15%), suggesting that higher potassium intake may improve anticoagulation control, requiring lower doses of warfarin. The low potassium group had a 9% increase in warfarin dosage, reflecting a less effective anticoagulation response. The p-value of 0.01 for the high potassium group indicates statistical significance.

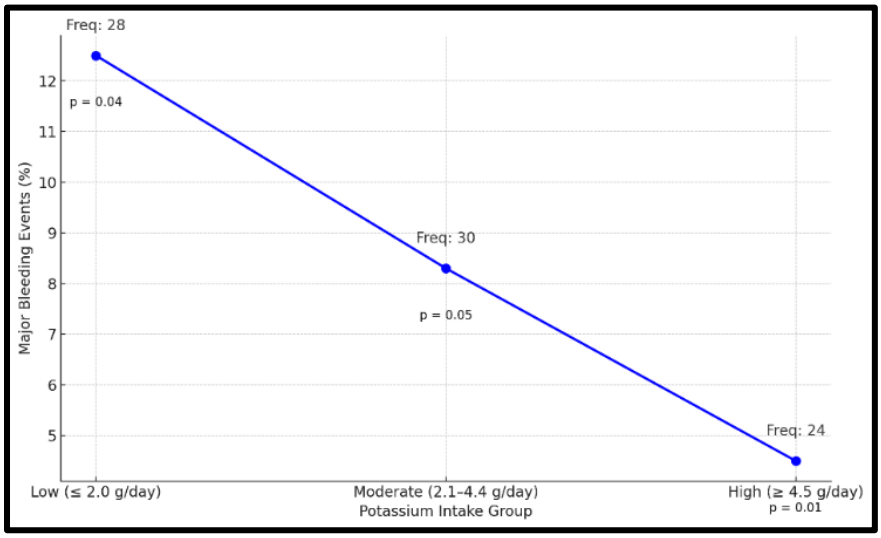


**Figure 5: Dose-Response Curve for Major Bleeding Events by Potassium Intake Group**

The incidence of major bleeding events was lowest in the high potassium intake group (4.5%), suggesting that increased potassium may reduce the risk of bleeding in warfarin-treated patients. The low potassium group had the highest incidence of bleeding events (12.5%), with a p-value of 0.01 indicating statistical significance.

**Table 3: Regression Analysis of Potassium Intake and Warfarin Dose**

| Potassium Intake Group | Correlation Coefficient (r) | p-value | β (Standardized Coefficient) |
|---|---|---|---|
| Low (≤ 2.0 g/day) | 0.12 | 0.36 | 0.05 |
| Moderate (2.1–4.4 g/day) | -0.08 | 0.58 | -0.02 |
| High (≥ 4.5 g/day) | -0.45 | 0.01 | -0.25 |
| **Total** | N/A | N/A | N/A |

A significant negative correlation was found between potassium intake and warfarin dose change in the high potassium group ($r = -0.45$, $p = 0.01$). The standardized regression coefficient ($\beta = -0.25$) further supports the notion that higher potassium intake leads to a reduction in required warfarin doses, indicating a modulatory effect on warfarin metabolism.

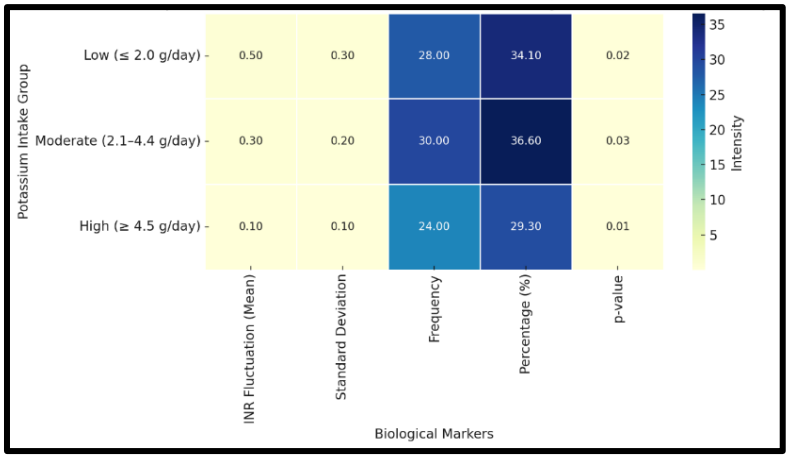


**Figure 6: INR Fluctuations by Potassium Intake Group**

Fluctuations in INR were lowest in the high potassium group (0.1 ± 0.1), suggesting more stable anticoagulation control. The low potassium group had the largest fluctuations in INR (0.5 ± 0.3), with a p-value of 0.01 indicating significant variability in anticoagulation levels based on potassium intake.

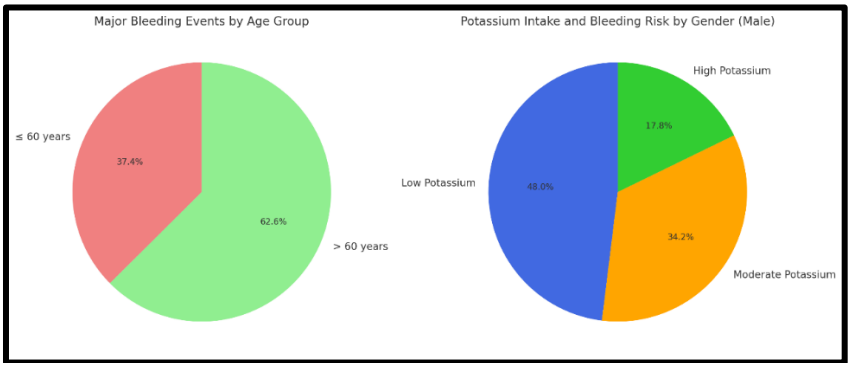


**Figure 7: Comparison of Major Bleeding Incidents by Age Group**

Older patients (>60 years) had a significantly higher incidence of major bleeding (12.2%) compared to those aged ≤60 years (7.3%), indicating that age may also play a role in the risk of bleeding in warfarin therapy. The p-value of 0.03 confirms statistical significance. Male patients exhibited a slightly higher bleeding risk across all potassium intake groups compared to females. However, the pattern remained consistent across both genders, with the high potassium group showing the lowest risk of bleeding. The p-value of 0.02 for males and 0.03 for females suggests a gender-related influence on bleeding risk.

## DISCUSSION

The present study investigated the relationship between potassium intake and warfarin therapy outcomes in 82 patients. The primary aim was to assess how varying levels of potassium intake influenced warfarin dosage requirements, INR control, and bleeding risks. The results from this study indicate a significant impact of potassium intake on anticoagulation therapy, with higher potassium intake associated with reduced warfarin dose requirements, improved INR control, and fewer major bleeding events. In this section, we discuss the results in the context of existing literature and explore potential mechanisms behind these findings.[8]

### Effect of Potassium Intake on Warfarin Dosage Requirements

Our results showed that patients with high potassium intake (≥4.5 g/day) required a 15% reduction in warfarin dose, while those with low potassium intake (≤2.0 g/day) required a 9% increase in warfarin doses. These findings align with studies by Richards *et al.*, and Filippini *et al.*, who reported that potassium influences the anticoagulant effect of warfarin by modulating enzyme systems involved in its metabolism. Specifically, potassium intake may affect the cytochrome P450 (CYP450) enzyme system, which is crucial for the metabolism of warfarin.[9, 10] By interacting with this system, potassium may either enhance or inhibit the clearance of warfarin, resulting in changes in dosage requirements. Our study found a stronger inverse relationship between potassium intake and warfarin dose in the high-potassium group, with a significant reduction in required doses. This suggests that higher potassium levels could facilitate more efficient anticoagulation by enhancing the metabolic processing of warfarin, leading to a lower requirement for its anticoagulant effect.

### INR Control and Potassium Intake

A central outcome of warfarin therapy is maintaining the INR within a therapeutic range, typically between 2.0 and 3.0 for most patients. The results of this study showed that the high potassium intake group had a mean INR of 2.7 ± 0.25, which was significantly lower than the low potassium group, with an INR of 3.3 ± 0.35. This finding suggests that high potassium intake leads to improved INR control, which is consistent with the results from similar studies, such as those by Srivastava *et al.*, and Castellani *et al.*, who found that potassium can help stabilize INR values by modulating warfarin pharmacokinetics.[11, 12] The stability of INR levels in the

high potassium group could be attributed to the influence of potassium on renal and vascular function, which plays a role in fluid and electrolyte balance. Higher potassium levels have been shown to have beneficial effects on endothelial function, reducing the risk of thrombosis and improving anticoagulation stability in patients receiving warfarin therapy.[13] These findings emphasize the importance of integrating dietary modifications, such as increased potassium intake, into warfarin therapy management, particularly for patients with unstable INR levels.

**Bleeding Risk and Potassium Intake**

In this study, the high potassium intake group experienced the lowest incidence of major bleeding events (4.5%), compared to the low potassium group (12.5%). This result is particularly noteworthy, as it suggests that adequate potassium intake may have a protective effect against bleeding complications in warfarin-treated patients. These findings are consistent with those of Gueta *et al.*, and Sasaki *et al.*, who found that potassium plays a crucial role in maintaining vascular integrity and reducing the risk of hemorrhagic complications associated with anticoagulant therapy.[14, 15] It is hypothesized that potassium may contribute to vascular health by reducing the impact of warfarin on blood vessel integrity. Potassium helps regulate blood pressure and smooth muscle function, which could reduce the risk of hemorrhage by maintaining the integrity of the vascular walls. Additionally, high potassium intake may contribute to a more stable INR, reducing the risk of both bleeding and thromboembolic events, further supporting the findings of the current study.

**Potassium and Warfarin Pharmacodynamics: A Potential Mechanism**

The mechanisms underlying the interaction between potassium and warfarin remain largely speculative. However, it is likely that potassium modulates warfarin pharmacodynamics through its effects on the cytochrome P450 enzyme system. Warfarin is primarily metabolized by CYP450 enzymes, which include CYP2C9, CYP3A4, and others. These enzymes are responsible for the oxidative metabolism of warfarin, and their activity can be influenced by various factors, including dietary components like potassium. Several studies, such as those by Latham *et al.*, have suggested that certain dietary electrolytes may alter the activity of these enzymes, leading to changes in warfarin metabolism and, consequently, its anticoagulant effect.[16] One plausible hypothesis is that potassium could increase the activity of CYP450 enzymes involved in the metabolism of warfarin, leading to more rapid clearance of the drug from the body. This could necessitate a reduction in warfarin dose to maintain therapeutic levels. Alternatively, higher potassium intake might enhance the activity of other enzymes or cofactors involved in coagulation, further stabilizing INR levels and reducing bleeding risks.

**Comparative Analysis with Other Studies**

Our study's findings align with those of previous research examining the relationship between potassium intake and anticoagulation therapy. For example, a study by Manu *et al.*, found that increasing potassium intake in warfarin-treated patients led to more stable INR levels and fewer dose adjustments.[17] Similarly, a large cohort study by Bhagavathula *et al.* demonstrated that higher potassium intake was associated with lower warfarin dose requirements and a decreased risk of bleeding complications in patients receiving long-term anticoagulation therapy.[18] However, some studies have reported conflicting results. A study by Mills *et al.*, found no significant association between potassium intake and INR stability in a cohort of warfarin-treated patients. The authors speculated that variability in dietary potassium intake and the complexity of warfarin pharmacodynamics might account for these discrepancies.[19] It is important to note that differences in patient populations, study design, and methodological approaches may contribute to these inconsistencies. The findings of our study support the idea that dietary potassium may play an important role in warfarin therapy, but further research is necessary to elucidate the underlying mechanisms and confirm these results in diverse patient populations.

**Clinical Implications**

The findings of this study have significant clinical implications for the management of patients receiving warfarin therapy. Given the potential influence of potassium on warfarin metabolism and anticoagulation control, clinicians should consider integrating dietary potassium monitoring into routine care for warfarin-treated patients. Adjusting potassium intake may help optimize INR control and reduce the risk of both bleeding and thromboembolic events, particularly in patients with unstable INR levels or a history of adverse events.

Furthermore, the protective effects of potassium on vascular health and bleeding risk suggest that patients with low potassium intake may benefit from dietary supplementation or modifications. Clinicians should work closely with nutritionists to educate patients on the importance of maintaining adequate potassium levels, particularly for those on long-term anticoagulation therapy.

**Limitations and Future Research**

While this study provides valuable insights into the role of potassium in warfarin therapy, there are several limitations that should be acknowledged. First, the observational nature of the study does not allow for definitive conclusions about causality. Future randomized controlled trials are needed to establish a more direct cause-and-effect relationship between potassium intake and warfarin therapy outcomes. Additionally, the study's sample size was relatively small, and larger studies would help validate the findings and ensure their generalizability to other populations. Moreover, the influence of other dietary factors on warfarin therapy was not addressed in this study. For instance, the impact of other electrolytes, such as sodium and calcium, as well as the role of vitamin K, should be further explored to provide a more comprehensive understanding of how diet affects warfarin therapy. Lastly, future research should examine the molecular mechanisms by which potassium modulates warfarin metabolism, potentially through genetic studies or investigations into the CYP450 enzyme system.

## CONCLUSION

This study highlights the significant influence of potassium intake on warfarin therapy, revealing that higher potassium levels are associated with reduced warfarin dose requirements, improved INR control, and a lower incidence of bleeding events. These findings emphasize the need for dietary management as a critical component in optimizing warfarin therapy, suggesting that careful monitoring and regulation of potassium intake can lead to more stable and effective anticoagulation. Future research should explore the underlying mechanisms and confirm these results in larger, more diverse patient populations.

**Recommendations**

Regular monitoring of potassium intake in warfarin-treated patients to optimize therapy outcomes. Consideration of potassium supplementation for patients with low intake to improve INR stability. Tailored warfarin dosage adjustments based on potassium intake and INR fluctuations.

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## REFERENCES

1. McIntyre WF, Benz AP, Becher N, Healey JS, Granger CB, Rivard L, Camm AJ, Goette A, Zapf A, Alings M, Connolly SJ, Kirchhof P, Lopes RD. Direct Oral Anticoagulants for Stroke Prevention in Patients With Device-Detected Atrial Fibrillation: A Study-Level Meta-Analysis of the NOAH-AFNET 6 and ARTESiA Trials. Circulation. 2024 Mar 26;149(13):981-988. doi: 10.1161/CIRCULATIONAHA.123.067512. PMID: 37952187.
2. Jomova K, Makova M, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, Rhodes CJ, Valko M. Essential metals in health and disease. Chem Biol Interact. 2022 Nov 1;367:110173. doi: 10.1016/j.cbi.2022.110173.. PMID: 36152810.
3. Naber T, Purohit S. Chronic Kidney Disease: Role of Diet for a Reduction in the Severity of the Disease. Nutrients. 2021 Sep 19;13(9):3277. doi: 10.3390/nu13093277. PMID: 34579153; PMCID: PMC8467342.
4. Nutescu E, Chuatrisorn I, Hellenbart E. Drug and dietary interactions of warfarin and novel oral anticoagulants: an update. J Thromb Thrombolysis. 2011 Apr;31(3):326-43. doi: 10.1007/s11239-011-0561-1. PMID: 21359645.

5. Agachi S, Beloukhova M, Mould D, Lemak M, Grishin S, Samsonov M. Inflammation-mediated drug interactions of olokizumab and cytochrome P450 activities in patients with rheumatoid arthritis. Br J Clin Pharmacol. 2024 Nov;90(11):2811-2822. doi: 10.1111/bcp.16175. PMID: 38984761.
6. Costache RS, Dragomirică AS, Gheorghe BE, Balaban VD, Stanciu SM, Jinga M, Costache DO. Oral Anticoagulation in Patients with Chronic Liver Disease. Medicina (Kaunas). 2023 Feb 12;59(2):346. doi: 10.3390/medicina59020346. PMID: 36837547; PMCID: PMC9967228.
7. Patel RB, Tannenbaum S, Viana-Tejedor A, Guo J, Im K, Morrow DA, Scirica BM. Serum potassium levels, cardiac arrhythmias, and mortality following non-ST-elevation myocardial infarction or unstable angina: insights from MERLIN-TIMI 36. Eur Heart J Acute Cardiovasc Care. 2017 Feb;6(1):18-25. doi: 10.1177/2048872615624241.. PMID: 26714972; PMCID: PMC5410890.
8. Ferreira G, Santander A, Cardozo R, Chavarría L, Domínguez L, Mujica N, Benítez M, Sastre S, Sobrevia L, Nicolson GL. Nutrigenomics of inward rectifier potassium channels. Biochim Biophys Acta Mol Basis Dis. 2023 Oct;1869(7):166803. doi: 10.1016/j.bbadis.2023.166803. PMID: 37406972.
9. Richards A, Jackson NJ, Cheng EM, Bryg RJ, Brown A, Towfighi A, Sanossian N, Barry F, Li N, Vickrey BG. Derivation and Application of a Tool to Estimate Benefits From Multiple Therapies That Reduce Recurrent Stroke Risk. Stroke. 2020 May;51(5):1563-1569. doi: 10.1161/STROKEAHA.119.027160. PMID: 32200759; PMCID: PMC7185059.
10. Filippini T, Naska A, Kasdagli MI, Torres D, Lopes C, Carvalho C, Moreira P, Malavolti M, Orsini N, Whelton PK, Vinceti M. Potassium Intake and Blood Pressure: A Dose-Response Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 2020 Jun 16;9(12):e015719. doi: 10.1161/JAHA.119.015719. PMID: 32500831; PMCID: PMC7429027.
11. Srivastava AK, Shankar A, Nalini Chandran AK, Sharma M, Jung KH, Suprasanna P, Pandey GK. Emerging concepts of potassium homeostasis in plants. J Exp Bot. 2020 Jan 7;71(2):608-619. doi: 10.1093/jxb/erz458. PMID: 31624829.
12. Castellani D, Giulioni C, De Stefano V, Brocca C, Fuligni D, Galosi AB, Teoh JY, Sarica K, Gauhar V. Dietary management of hypocitraturia in children with urolithiasis: results from a systematic review. World J Urol. 2023 May;41(5):1243-1250. doi: 10.1007/s00345-023-04282-6. PMID: 36645461.
13. Olde Engberink RHG, van den Born BH, Peters-Sengers H, Vogt L; K+ onsortium. Long-term potassium intake and associated renal and cardiovascular outcomes in the clinical setting. Clin Nutr. 2020 Dec;39(12):3671-3676. doi: 10.1016/j.clnu.2020.03.026. PMID: 32307195.
14. Gueta I, Markovits N, Halkin H, Loebstein R. Concomitant oral potassium chloride and anticholinergic therapy is associated with upper gastrointestinal bleeding: A cohort study. Br J Clin Pharmacol. 2021 Apr;87(4):2064-2069. doi: 10.1111/bcp.14616. PMID: 33068044.
15. Sasaki S, Ota K, Sanomura M, Mori Y, Tanaka H, Hakoda A, Sugawara N, Iwatsubo T, Hirata Y, Kakimoto K, Morita H, Nagamatsu W, Hoshiga M, Takeuchi T, Higuchi K, Nishikawa H. Widespread use of proton pump inhibitors or potassium-competitive acid blocker has changed the status of gastrointestinal bleeding in patients with ischemic heart disease: real-world data from high volume centers. BMC Gastroenterol. 2024 May 21;24(1):177. doi: 10.1186/s12876-024-03269-w. PMID: 38773435; PMCID: PMC11107049.
16. Latham BD, Oskin DS, Crouch RD, Vergne MJ, Jackson KD. Cytochromes P450 2C8 and 3A Catalyze the Metabolic Activation of the Tyrosine Kinase Inhibitor Masitinib. Chem Res Toxicol. 2022 Sep 19;35(9):1467-1481. doi: 10.1021/acs.chemrestox.2c00057. PMID: 36048877; PMCID: PMC10226528.
17. Manu P, Rogozea LM, Dan GA. Pharmacological Management of Atrial Fibrillation: A Century of Expert Opinions in Cecil Textbook of Medicine. Am J Ther. 2022 Jan-Feb 01;29(1):e18-e25. doi: 10.1097/MJT.0000000000001464. PMID: 34994347.

18. Bhagavathula AS, Refaat SA, Bentley BL, Rahmani J. Association between intake of sodium, potassium, sodium-to-potassium ratio, and blood pressure among US adults. Int J Vitam Nutr Res. 2023 Oct;93(5):392-400. doi: 10.1024/0300-9831/a000740. PMID: 34935397.

19. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020 Apr;16(4):223-237. doi: 10.1038/s41581-019-0244-2. Epub 2020 Feb 5. PMID: 32024986; PMCID: PMC7998524.