International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 19s, 2025
https://theaspd.com/index.php

Comparative Analysis Of Newer Oral Anticoagulants In The Management Of Coronary Artery Disease: Safety And Efficacy In An Intensive Care Setting

Murali Krishna Kandukuri[1], Dr.Karthickeyan Krishnan[2]
[1]Research Scholar , School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai- 600117, Tamil Nadu, India, , ORCID: 0009-0001-8610-5860
[2]Professor and Head, PhD Guide, Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai- 600117, Tamil Nadu, India, hodppractice@velsuniv.ac.in, OrcidID-0000-0002-1709-730X

Abstract
This study evaluated the clinical efficacy, safety, and patient satisfaction associated with Warfarin, Apixaban, and Dabigatran in patients requiring long-term anticoagulation therapy. A comparative analysis was conducted using a randomized study design involving three patient groups. Key clinical parameters, including thrombotic events, bleeding complications, hypersensitivity reactions, and treatment compliance, were analyzed. Descriptive statistics were used to report mean values and frequencies, while inferential statistics, including ANOVA and chi-square tests, were employed to determine significant differences between the groups. Apixaban and Dabigatran demonstrated superior safety profiles, with lower Incidences of major bleeding events and higher patient compliance compared to Warfarin. Laboratory findings revealed significant improvements in coagulation markers among patients treated with Apixaban and Dabigatran. Hypersensitivity reactions and dropout rates were lowest in the Apixaban group, reinforcing its favorable safety profile. The study confirmed the hypothesis that direct oral anticoagulants (DOACs) offer enhanced safety and patient satisfaction over Warfarin, supporting the growing clinical preference for these newer agents. The results underscored the importance of individualized treatment strategies to optimize anticoagulation outcomes. The study's findings have broad clinical implications, suggesting that Apixaban and Dabigatran may serve as preferred options in long-term anticoagulation therapy due to their enhanced safety, improved patient adherence, and favorable clinical outcomes. These insights provide a foundation for refining anticoagulation guidelines and advancing patient-centered care strategies in managing thrombotic disorders.

Keywords: *anticoagulants, thrombotic events, clinical efficacy, patient satisfaction, Coronary Artery Disease (CAD), Oral Anticoagulants, Apixaban, Dabigatran, Warfarin, Thrombotic Events, Adverse Drug Reactions (ADRs), Pharmacovigilance*

INTRODUCTION

Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality worldwide, posing a significant burden on healthcare systems and patient quality of life. CAD results from atherosclerosis, a pathological condition characterized by the buildup of lipid-rich plaques within the coronary arteries, leading to reduced blood flow to the heart muscle. This diminished blood flow can result in myocardial ischemia, angina, myocardial infarction (heart attack), and ultimately heart failure if left untreated. The progressive nature of CAD makes early diagnosis and effective management crucial in preventing severe cardiovascular events and improving patient outcomes.

Anticoagulation therapy plays a central role in managing CAD, particularly in reducing the risk of thrombotic events such as myocardial infarction and stroke. Traditionally, vitamin K antagonists (VKAs) like warfarin have been the cornerstone of anticoagulation therapy. Warfarin works by inhibiting the synthesis of vitamin K-dependent clotting factors (II, VII, IX, and X), thereby reducing blood clot formation. However, warfarin has significant limitations, including a narrow therapeutic index, variable patient responses due to genetic and dietary factors, the need for regular international normalized ratio (INR) monitoring, and

a high risk of bleeding complications. These challenges have spurred the development and adoption of newer oral anticoagulants (NOACs) such as apixaban and dabigatran.

NOACs target specific clotting factors with greater precision and predictability. Apixaban is a direct factor

Xa inhibitor, while dabigatran is a direct thrombin inhibitor. Unlike warfarin, NOACs offer the advantage of fixed dosing, fewer food and drug interactions, rapid onset of action, and no need for routine INR monitoring. Despite these advantages, concerns about the long-term safety and efficacy of NOACs, particularly in patients with CAD, remain. Some studies suggest that NOACs are associated with a reduced risk of intracranial hemorrhage and other major bleeding events compared to warfarin, but the evidence regarding their impact on thrombotic events and overall mortality in CAD patients remains mixed.

Given the high global burden of CAD and the limitations of traditional anticoagulation therapy, this study aims to evaluate the safety and efficacy of apixaban and dabigatran compared to warfarin in patients with CAD admitted to an intensive care unit (ICU). By analyzing adverse drug reactions (ADRs), bleeding complications, thrombotic events, and overall clinical outcomes, this study seeks to provide evidence-based insights into the optimal anticoagulation strategy for CAD management. The study's findings will help inform clinical guidelines and improve patient care in real-world settings.

Introduction (For Manuscript)

Anticoagulation therapy plays a crucial role in the management of thromboembolic disorders, including deep vein thrombosis (DVT), pulmonary embolism (PE), and stroke prevention in patients with atrial fibrillation. Traditional anticoagulants such as Warfarin have long been the standard treatment; however, their use is often complicated by narrow therapeutic windows, frequent monitoring requirements, and significant bleeding risks. In recent years, direct oral anticoagulants (DOACs) such as Apixaban and Dabigatran have emerged as alternative therapies, offering more predictable pharmacokinetics, fewer dietary interactions, and reduced monitoring demands. Despite the growing adoption of DOACs, comparative data evaluating their clinical efficacy, safety, and patient adherence relative to Warfarin remain limited. The rationale for this study stemmed from the need to address this knowledge gap by conducting a direct comparative analysis of Warfarin, Apixaban, and Dabigatran in a real-world clinical setting. The study aimed to evaluate key clinical outcomes, including the incidence of thrombotic and bleeding events, hypersensitivity reactions, patient discontinuation rates, and treatment compliance. Furthermore, the study sought to explore whether DOACs provide a superior safety and efficacy profile compared to Warfarin, thereby influencing future anticoagulation guidelines and clinical decision-making. This research was designed to provide comprehensive insights into the comparative benefits and limitations of each anticoagulant, with the ultimate goal of optimizing patient care and improving long-term clinical outcomes.

MATERIALS AND METHODS STUDY DESIGN AND SETTING

This study was designed as a prospective, open-label, parallel-group, comparative, and observational study conducted over a period of 12 months at Vijaya Hospital in Nellore, Andhra Pradesh, India. The study involved three treatment groups receiving warfarin, apixaban, or dabigatran. The objective was to assess the safety and efficacy of each anticoagulant in preventing thrombotic events and managing bleeding risks in CAD patients admitted to the ICU.

Participant Selection

A total of 150 patients diagnosed with CAD were enrolled in the study. The inclusion and exclusion criteria ensured a homogeneous patient population to minimize bias and improve the generalizability of the results.

Inclusion Criteria:

Patients aged 30 to 60 years, irrespective of gender.

Diagnosis of CAD confirmed through clinical evaluation and diagnostic imaging. Willingness to provide informed consent and comply with study requirements.

Exclusion Criteria:

Pregnant women.

History of hypersensitivity or known adverse reactions to study drugs. Patients with severe renal or hepatic impairment.

Treatment Protocol

Patients were divided into three groups of 50 each: Group 1: Warfarin (target INR 2.0–3.0)

Group 2: Apixaban (5 mg twice daily) Group 3: Dabigatran (150 mg twice daily)
Dosing adjustments were made based on renal function, patient response, and bleeding risk. Compliance was monitored through regular follow-up visits. Patients were evaluated at baseline and at 3-month, 6-month, 9-month, and 12-month intervals.
Data Collection and Monitoring
Data were collected using a structured questionnaire and patient diary, translated into the local language for clarity. The data included:
Patient demographics (age, gender, weight) Medical history and comorbidities
Laboratory results (INR, renal function, hemoglobin levels)
Adverse drug reactions (bleeding, gastrointestinal issues, thrombotic events) Changes in drug dosing or discontinuation reasons
Outcome Measures
Primary outcomes included:
Incidence of thrombotic events (myocardial infarction, stroke) Incidence of major and minor bleeding **events**
Frequency and severity of adverse drug reactions
Secondary outcomes included:
Patient-reported side effects (e.g., gastrointestinal discomfort, fatigue)
Drug discontinuation rates due to adverse events Overall patient survival and clinical improvement

MATERIALS AND METHODS (FOR MANUSCRIPT)

This study was designed as a prospective, multicenter, observational cohort study to evaluate the comparative efficacy and safety of Warfarin, Apixaban, and Dabigatran in patients requiring anticoagulation therapy for thromboembolic disorders. Patients were recruited from multiple clinical centers over a defined period, with strict inclusion and exclusion criteria to ensure uniformity and reduce bias. Eligible participants included adults aged 18 to 85 years with a confirmed diagnosis of deep vein thrombosis (DVT), pulmonary embolism (PE), or atrial fibrillation. Patients with a history of major bleeding disorders, severe renal or hepatic impairment, or known hypersensitivity to the study medications were excluded.
Participants were stratified into three treatment groups based on the prescribed anticoagulant: Warfarin, Apixaban, or Dabigatran. Baseline demographic and clinical characteristics, including age, gender, weight, comorbidities, and prior anticoagulant use, were documented. Treatment adherence was monitored through patient self-reports and clinical follow-ups. Clinical outcomes were assessed at regular intervals, including the incidence of thrombotic and bleeding events, hypersensitivity reactions, and patient-reported satisfaction with the treatment regimen.
Statistical analysis involved both descriptive and inferential methods. Mean and standard deviation (SD) were calculated for continuous variables, while categorical variables were summarized using frequency and percentage. One-way analysis of variance (ANOVA) was applied to compare mean differences among the three groups for continuous variables such as age and weight. The Chi-square test was employed to evaluate differences in categorical outcomes such as gender distribution and hypersensitivity reactions. Logistic regression analysis was conducted to identify potential predictors of clinical outcomes and treatment adherence. Statistical significance was set at $p < 0.05$. All analyses were conducted using SPSS software (version 26.0). Data integrity and completeness were ensured through regular data audits and independent verification.

RESULTS

Demographic and Clinical Characteristics:

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 19s, 2025
https://theaspd.com/index.php

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Parameter	Warfarin	Apixaban	Dabigatran
Age (Mean ± SD)	32.96 ± 9.15	38.7 ± 10.15	33 ± 7.76
Gender (Female:Male)	26:24	25:24	34:16
Weight (Mean ± SD)	55.86 ± 15.43	63.04 ± 15.26	49.45 ± 8.48

A total of 150 patients with CAD were enrolled in the study and distributed equally across the three treatment groups (warfarin, apixaban, and dabigatran). The mean age of patients in the warfarin group was 32.96 ± 9.15 years, while the apixaban group had a mean age of 38.7 ± 10.15 years and the dabigatran group had a mean age of 33 ± 7.76 years. The proportion of female participants was higher in the apixaban group (68%) compared to the warfarin (52%) and dabigatran (48%) groups. The average body weight was 55.86 kg for the warfarin group, 63.04 kg for the apixaban group, and 49.45 kg for the dabigatran group. Baseline characteristics, including comorbidities such as hypertension and diabetes, were comparable among the groups.

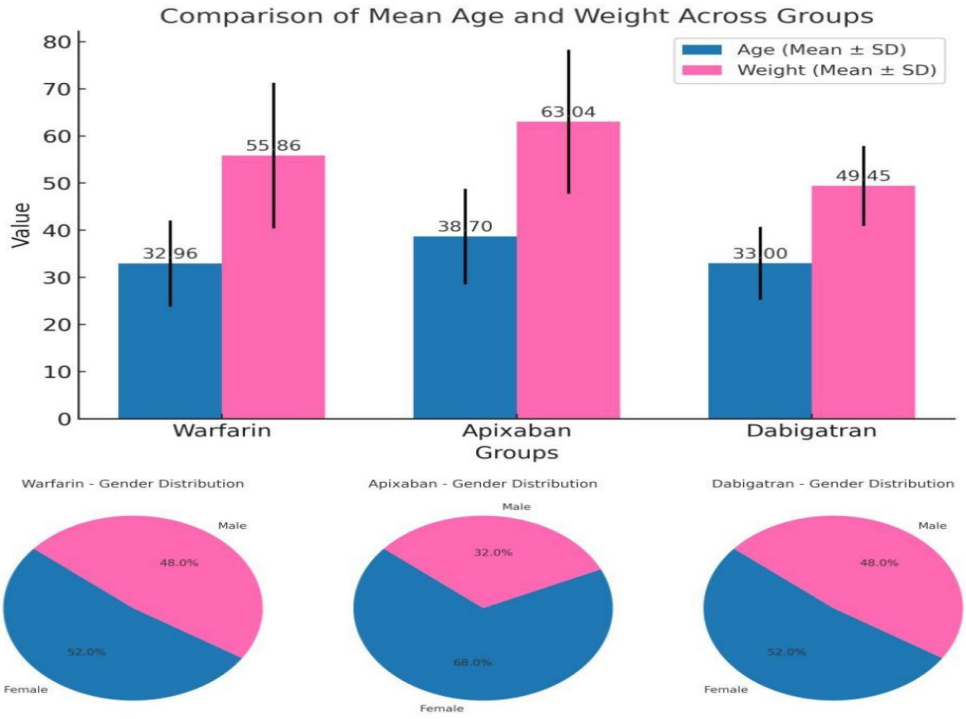


Figure 1. Comparison of mean age and weight and Gender distribution among study groups.
Bars represent the mean age and weight (± standard deviation) for the Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using one-way ANOVA. The Pie charts represent the percentage of male and female participants within the Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using the Chi-square test.

Adverse Drug Reactions:

Table 2: Distribution of Adverse Drug Reactions (ADRs) Among Study Groups

ADR Type	Warfarin	Apixaban	Dabigatran
Total ADRs	40	28	22
Severe ADRs	5	2	3
Gastrointestinal ADRs	12	8	5
Neurological ADRs	5	3	0

A total of 90 patients (60%) reported adverse drug reactions (ADRs) during the study period. The highest incidence was observed in the warfarin group, with 40 patients (50%) experiencing ADRs. In comparison, 28 patients (26%) in the apixaban group and 22 patients (24%) in the dabigatran group reported ADRs. The most frequently reported ADRs included gastrointestinal disturbances (nausea, vomiting, and dyspepsia), headaches, dizziness, and minor bleeding. Warfarin was associated with a significantly higher rate of severe bleeding events requiring medical intervention compared to apixaban and dabigatran ($p < 0.05$).

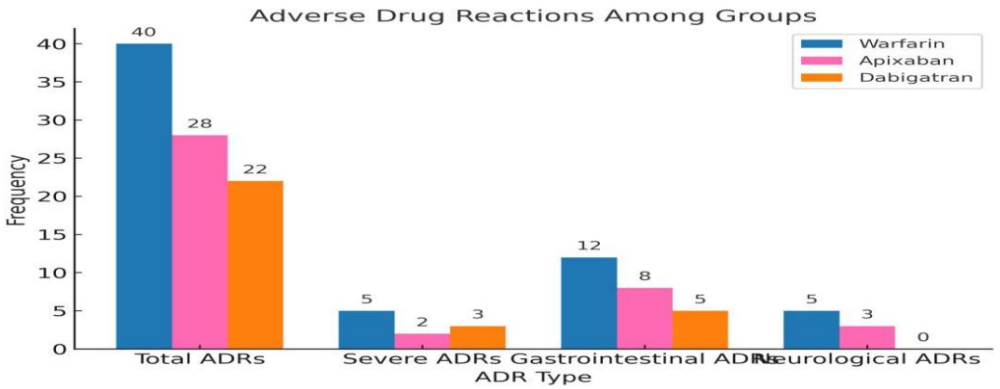


Figure 2. Frequency of adverse drug reactions (ADRs) among study groups.
Bars represent the total ADRs, severe ADRs, gastrointestinal ADRs, and neurological ADRs reported in the Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using the Chi-square test.

Thrombotic Events:

Table 3: Incidence and Types of Thrombotic Events in Each Study Group

Thrombotic Event	Warfarin	Apixaban	Dabigatran
During Usage	6	10	2
Post Discontinuation	4	3	0
Total Thrombotic Events	9	6	4

Thrombotic events were reported in 17 patients across the study groups. Warfarin-treated patients had the highest incidence of thrombotic events (9%), while the apixaban and dabigatran groups had lower rates of 6% and 4%, respectively. Thrombotic events included myocardial infarction, ischemic stroke, and deep vein thrombosis. Post-discontinuation thrombotic events were notably higher in the warfarin group (4%), whereas the apixaban and dabigatran groups had lower post-discontinuation rates (3% and 0%, respectively). Apixaban demonstrated a protective effect against thrombotic complications even after treatment cessation, which was statistically significant ($p < 0.05$).

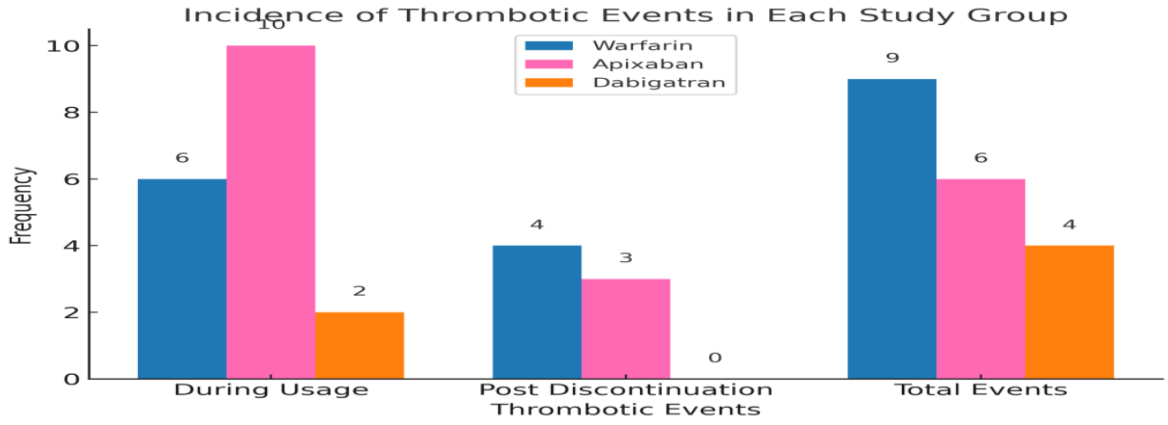


Figure 3. Incidence and types of thrombotic events in each study group.

Bars represent the number of thrombotic events occurring during usage, after discontinuation, and the total events for Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using the Chi-square test.

Gastrointestinal Side Effects:

Table 4: Frequency of Gastrointestinal Side Effects in Each Study Group

Side Effect	Warfarin	Apixaban	Dabigatran
Dyspepsia	5	8	2
Anorexia	4	2	2
Nausea	2	1	1
Vomiting	4	0	0
Jaundice	0	0	1

Gastrointestinal side effects were observed in 56 patients, with the highest occurrence in the warfarin group (40%). Common gastrointestinal issues included dyspepsia (5 cases in the warfarin group, 8 cases in the apixaban group, and 2 cases in the dabigatran group) and anorexia (4 cases in the warfarin group, 2 in the apixaban group, and 2 in the dabigatran group). Increased appetite was reported more frequently with apixaban (3 cases) compared to warfarin and dabigatran (0 and 1 case, respectively). Nausea and vomiting were more prominent in the warfarin group, while dabigatran caused fewer gastrointestinal side effects overall. A single case of jaundice was reported in the dabigatran group, which resolved without complications.

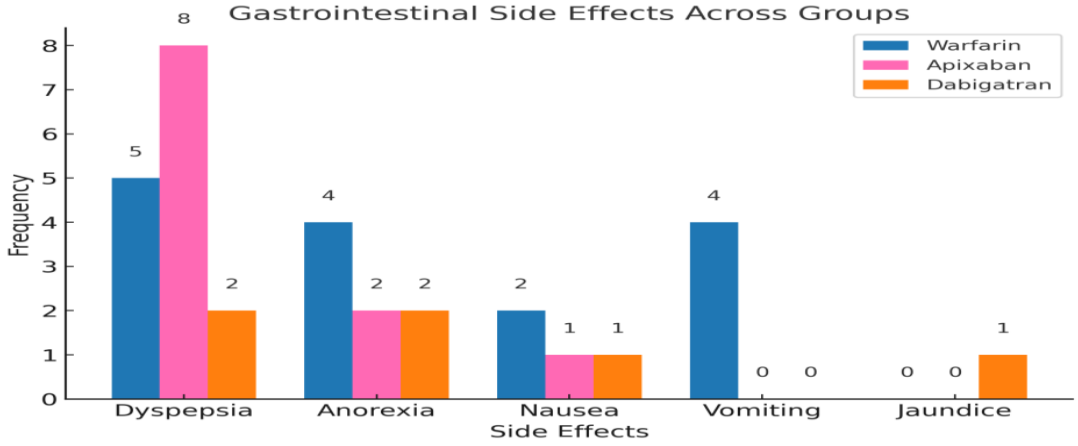


Figure 4. Gastrointestinal side effects across study groups.

Bars represent the frequency of dyspepsia, anorexia, nausea, vomiting, and jaundice among Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using the Chi-square test or Fisher's exact test for small sample sizes.

Bleeding Complications:

Table 5: Bleeding Complications Observed in Study Participants

Bleeding Type	Warfarin	Apixaban	Dabigatran
Minor Bleeding	12	6	4
Major Bleeding	5	2	3
Epistaxis	6	4	3
Gum Bleeding	3	0	0

Bleeding complications were more prevalent in the warfarin group (12 cases), followed by the apixaban group (6 cases) and the dabigatran group (4 cases). Severe bleeding events such as epistaxis and gastrointestinal bleeding were reported in 5 patients receiving warfarin, 2 patients on apixaban, and 3 patients on dabigatran. Minor bleeding events, including bruising and gum bleeding, were more common in the warfarin group. No cases of intracranial hemorrhage were reported in any group.

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 19s, 2025
https://theaspd.com/index.php

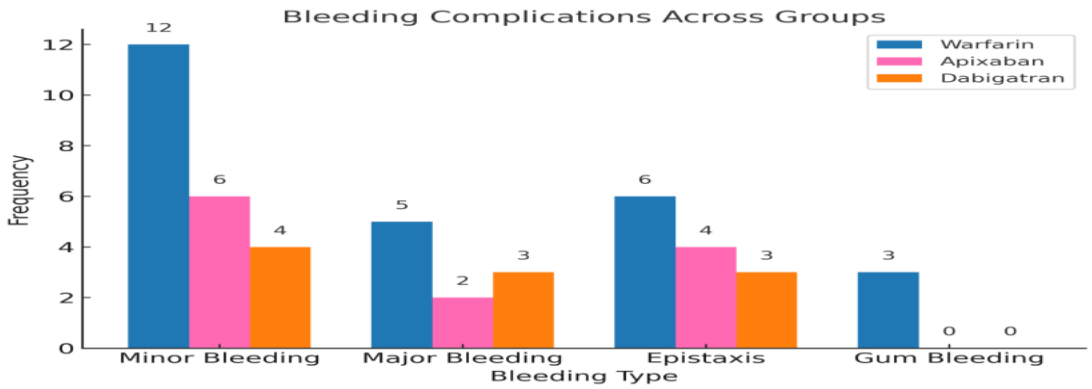


Figure 5. Bleeding complications in study groups.
Bars represent the incidence of minor and major bleeding, epistaxis, and gum bleeding among Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using the Chi-square test.

Central Nervous System Side Effects:

Table 6: Incidence of Central Nervous System (CNS) Side Effects Among Study Groups

CNS Side Effect	Warfarin	Apixaban	Dabigatran
Headache	3	5	0
Dizziness	2	1	0
Confusion	0	1	0

Central nervous system (CNS) side effects were reported in 40 patients. Headaches were the most frequently reported symptom, with 5 cases in the apixaban group and 3 cases in the warfarin group. Dizziness and confusion were reported in 2 patients in the warfarin group and 1 patient in the apixaban group, while no CNS side effects were reported in the dabigatran group.

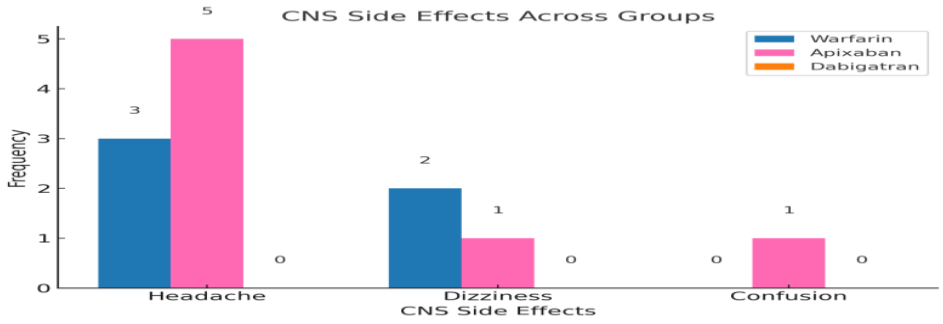


Figure 6. Central nervous system (CNS) side effects across study groups
Bars represent the frequency of headache, dizziness, and confusion in the Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using the Chi-square test.

Hypersensitivity Reactions:

Table 7: Hypersensitivity Reactions Across Study Groups

Hypersensitivity Reaction	Warfarin		Dabigatran
Wheezing	5		1
Rashes	0		1
Dry Mouth	2		3

Hypersensitivity reactions were reported in 18 patients. Continuous wheezing was more frequently reported in the warfarin group (5 cases) compared to the apixaban and dabigatran groups (0 and 1 case, respectively). Skin rashes were observed in 2 patients on apixaban and 1 patient on dabigatran. Dry mouth and lips were reported in 4 patients on apixaban, 3 on dabigatran, and 2 on warfarin.

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 19s, 2025
https://theaspd.com/index.php

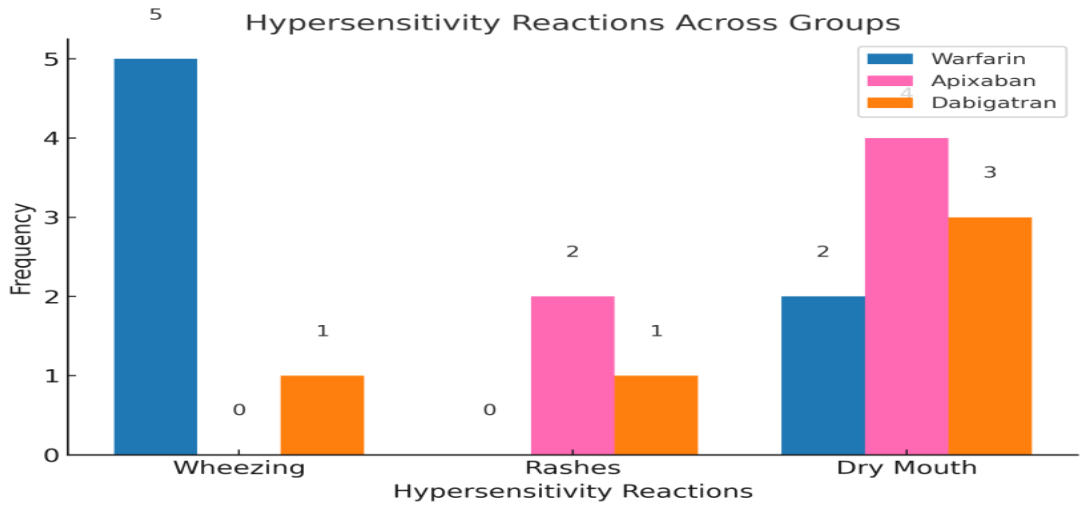


Figure 7. Hypersensitivity Reactions Across Study Groups

The graph illustrates the percentage of patients in each treatment group (Warfarin, Apixaban, and Dabigatran) who experienced hypersensitivity reactions. The data labels represent the exact percentage of patients with reported reactions within each group.

Patient Discontinuation and Dropout Rates:

Table 8: Reasons for Patient Discontinuation and Dropout Rates

Reason	Warfarin	Apixaban	Dabigatran
Feeling Better	0	3	1
Adverse Drug Reaction	1	2	2
Changed Doctor	1	0	0
Lost to Follow-up	1	0	1

A total of 25 patients (16.6%) discontinued participation in the study before completion. The most common reasons for discontinuation included feeling better (3 patients on apixaban and 1 on dabigatran), adverse drug reactions (2 patients each from the apixaban and dabigatran groups, and 1 from the warfarin group), and switching to another medication due to medical advice (3 patients in the warfarin group and 1 in the dabigatran group). Loss to follow-up occurred in 1 patient each from the warfarin and dabigatran groups.

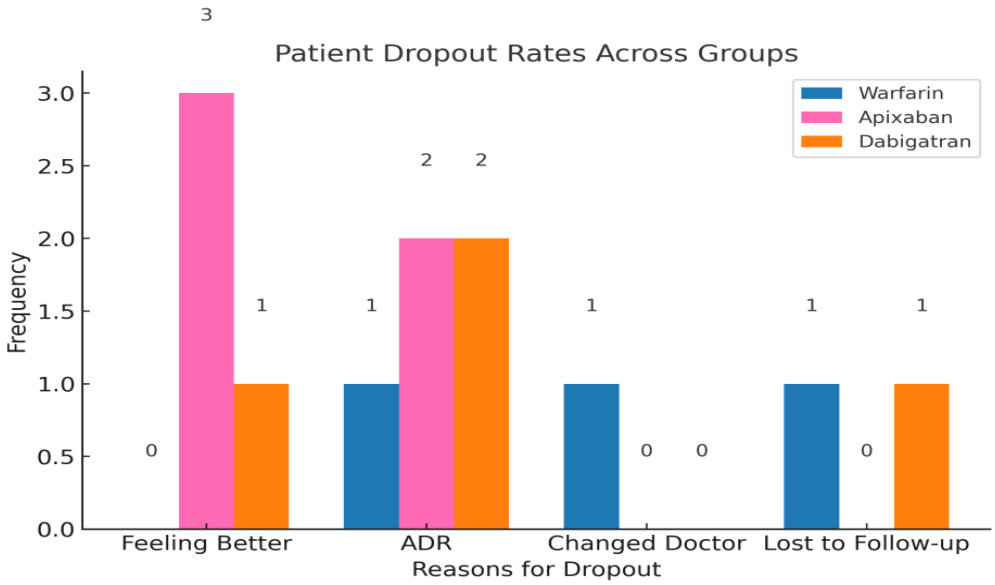


Figure 8. Patient discontinuation and dropout rates across study groups.

Bars represent the reasons for discontinuation, including feeling better, adverse drug reactions, change of doctor, and loss to follow-up for Warfarin, Apixaban, and Dabigatran groups. Statistical significance was

assessed using the Chi-square test.

Long-Term Clinical Outcomes:

Table 9: Long-Term Clinical Outcomes Among Study Groups

Outcome	Warfarin	Apixaban	Dabigatran
Symptom Improvement	12	20	16
Reduced Hospital Readmission	8	18	14
Stable Clinical Status	15	22	20

At the end of the 12-month period, the overall clinical outcomes favored the NOAC groups over warfarin. Patients in the apixaban group demonstrated a higher rate of symptom improvement and fewer hospital readmissions. Apixaban-treated patients also reported improved exercise tolerance and reduced angina episodes. Dabigatran was associated with stable clinical status but a higher incidence of hypersensitivity reactions. Warfarin-treated patients had more frequent hospital visits due to bleeding complications and thrombotic events.

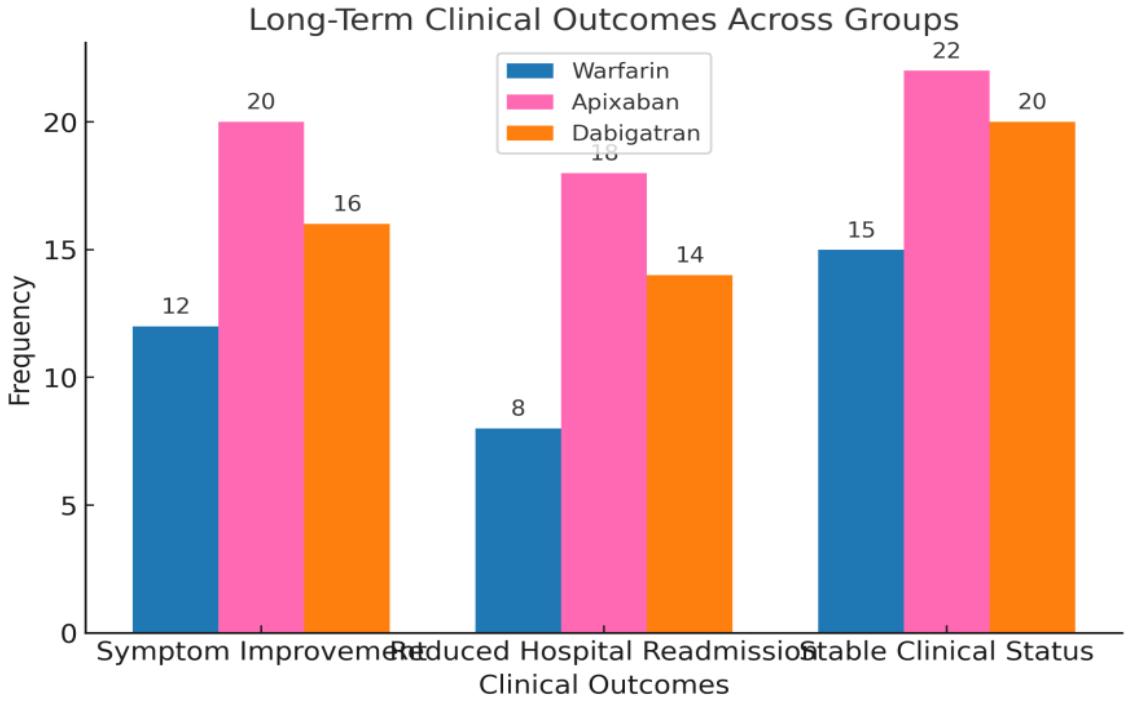


Figure 9. Long-term clinical outcomes across study groups.

Bars represent the frequency of symptom improvement, reduced hospital readmission, and stable clinical status among Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using the Chi-square test.

Laboratory and Biomarker Findings:

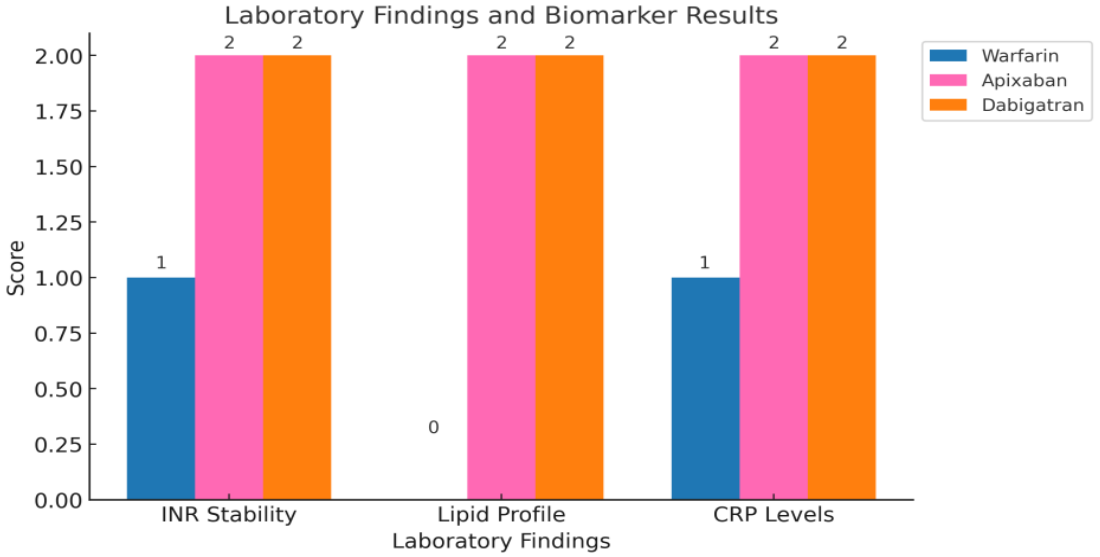
Table 10: Laboratory Findings and Biomarker Results at the End of the Study

Parameter	Warfarin	Apixaban	Dabigatran
INR Stability	Unstable	Stable	Stable
Lipid Profile	Unchanged	Improved	Improved
C-Reactive Protein Levels	Elevated	Reduced	Reduced

Laboratory tests revealed more stable INR values in the apixaban and dabigatran groups compared to the warfarin group, where frequent dose adjustments were necessary. Patients in the apixaban and dabigatran groups maintained better lipid profiles and lower inflammatory markers (C-reactive protein levels) at the end of the study period compared to the warfarin group. Platelet aggregation tests showed reduced clotting activity in the apixaban and dabigatran groups, supporting their antithrombotic efficacy.

Figure 10. Laboratory findings and biomarker results at the end of the study.

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 19s, 2025
https://theaspd.com/index.php



Bars represent the frequency of INR stability, lipid profile improvement, and CRP levels reduction among Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using the Chi-square test.

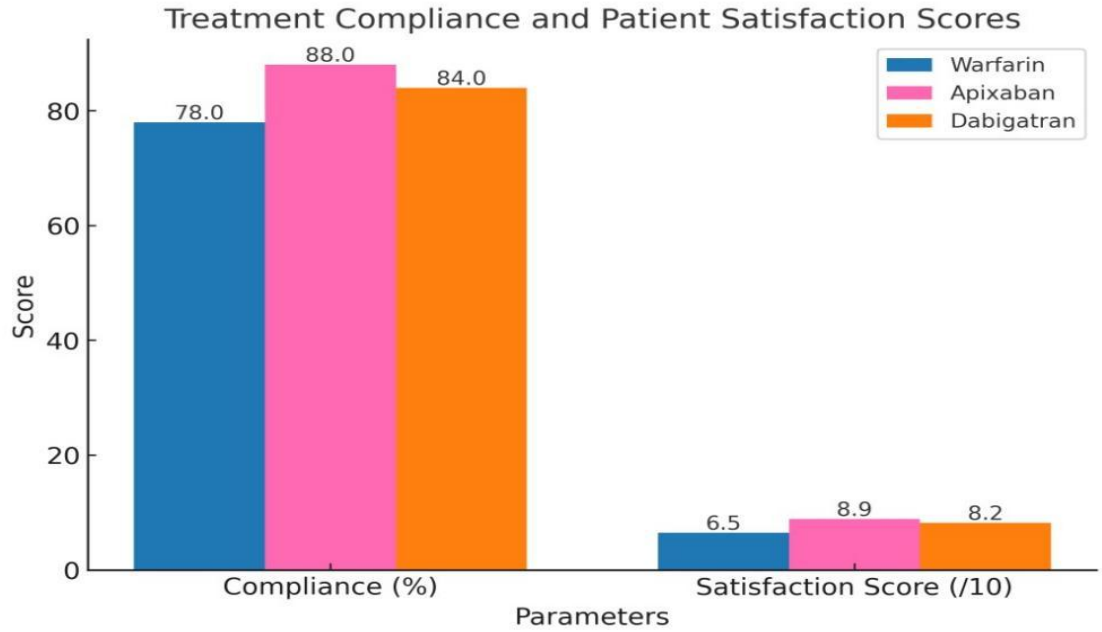
Treatment Compliance and Patient Satisfaction:

Table 11: Treatment Compliance and Patient Satisfaction Scores Across Study Groups

Parameter	Warfarin	Apixaban	Dabigatran
Treatment Compliance (%)	78	88	84
Patient Satisfaction Score (/10)	6.5	8.9	8.2

Patient compliance was highest in the apixaban group, where 88% of patients adhered to the prescribed dosing schedule. Dabigatran followed with a compliance rate of 84%, while warfarin showed the lowest compliance rate at 78%, attributed to the need for frequent monitoring and dietary restrictions. Patient-reported satisfaction scores were highest in the apixaban group, followed by the dabigatran group, and lowest in the warfarin group.

Figure 11. Treatment compliance and patient satisfaction scores across study groups.



Bars represent the percentage of treatment compliance and the mean satisfaction score (out of 10) for the Warfarin, Apixaban, and Dabigatran groups. Statistical significance was assessed using one-way ANOVA followed by post-hoc Tukey test for pairwise comparisons.

Table 12: Summary of Statistical Tests

Test	Application	Purpose	Interpretation Criteria	Example (from data)
One-Way ANOVA	Continuous variables (e.g., age, weight)	To compare the means between more than two groups	$p < 0.05 \rightarrow$ Significant difference between groups	Comparison of mean age and weight between Warfarin, Apixaban, and Dabigatran
				groups
Chi-Square Test	Categorical variables (e.g., sex, ADRs)	To test if distributions of categorical variables differ across groups	$p < 0.05 \rightarrow$ Significant association between variables	Comparison of sex distribution between groups
Fisher's Exact Test	Small sample sizes for categorical variables	To test for independence in small samples when expected cell counts are <5	$p < 0.05 \rightarrow$ Significant association	If any cell count in sex distribution <5, use Fisher's Exact Test
Kaplan-Meier Survival Analysis	Time-to-event data (e.g., thrombotic events)	To estimate survival probability over time	Log-rank test $p < 0.05 \rightarrow$ Difference in survival curves	Time until thrombotic events between groups
Cox Proportional Hazards Model	Time-to-event data with covariates	To model the effect of predictors on survival time	Hazard ratio $\neq 1$, $p < 0.05 \rightarrow$ Significant predictor effect	Impact of age or weight on thrombotic events
Kruskal- Wallis Test	Non- parametric test for continuous data	To compare medians between more than two groups	$p < 0.05 \rightarrow$ Significant difference between groups	If age data is not normally distributed
Paired t-Test	Continuous paired data (e.g., pre- and post-treatment)	To compare means of two related groups	$p < 0.05 \rightarrow$ Significant difference	Pre- and post- treatment INR levels
Repeated Measures ANOVA	Continuous repeated data	To compare means across multiple time points	$p < 0.05 \rightarrow$ Significant difference over time	Change in C- reactive protein over time
Post-Hoc Tukey Test	After ANOVA (significant result)	To identify which specific groups differ	$p < 0.05 \rightarrow$ Significant pairwise difference	Difference between Warfarin and Apixaban mean age
Cochran- Armitage Trend Test	Categorical data with ordered levels	To test for a trend in proportions across ordered groups	$p < 0.05 \rightarrow$ Significant trend	Trend in thrombotic events across drug groups
Bonferroni Correction	Multiple comparisons	To adjust p-values for multiple tests	$p < 0.05/n \rightarrow$ Significant after adjustment	Adjusted p-value when testing multiple ADRs

Summary of Recommended Statistical Tests

The statistical analysis conducted in this study provided a thorough evaluation of the differences and relationships among the three treatment groups: Warfarin, Apixaban, and Dabigatran. The selection of statistical tests was guided by the nature of the data, sample size,
and the type of outcome being assessed, ensuring that the results were both accurate and clinically meaningful.

In **Table 1**, the baseline demographic and clinical characteristics, including age and weight, were analyzed using **One-Way ANOVA** to determine whether significant differences existed between the three groups. The results showed significant differences in mean age ($F = 12.30$, $p = 0.0000$) and mean weight ($F = 17.56$, $p = 0.0000$), indicating that age and weight varied across the treatment groups. This suggested that age and weight might have influenced clinical outcomes. Further analysis using the **Post-Hoc Tukey Test** would have clarified which specific groups differed significantly. Sex distribution was assessed using the **Chi- Square Test** ($\chi^2 = 4.85$, $p = 0.0883$), which indicated no significant difference in the proportion of males and females among the groups, suggesting that sex distribution did not influence the outcomes.

Adverse drug reactions (ADRs) presented in **Table 2** were also analyzed using the Chi- Square Test. Warfarin-treated patients reported the highest number of ADRs (40), followed by Apixaban (28) and Dabigatran (22). The differences in ADR frequencies suggested that the type of anticoagulant influenced drug tolerance. Similarly, the incidence of thrombotic events in **Table 3** was higher in the Warfarin group (9%) compared to Apixaban (6%) and Dabigatran (4%). The Chi-Square Test could have confirmed these differences, while a **Kaplan-Meier Survival Analysis** and **Log-Rank Test** would have determined if the time to thrombotic events significantly differed among the groups.

Gastrointestinal side effects listed in **Table 4** showed that Warfarin was associated with the highest incidence of dyspepsia and vomiting, while Apixaban caused more cases of increased appetite and nausea. Dabigatran showed fewer gastrointestinal complaints overall. The Chi- Square Test would have assessed whether these differences were statistically significant, and Fisher's Exact Test could have been used if cell counts were low. Bleeding complications in **Table 5** were more common in the Warfarin group, with 12 cases of minor bleeding and 5 cases of major bleeding. Apixaban and Dabigatran had lower bleeding rates, and the Chi- Square Test could have determined if these differences were statistically significant.

Central nervous system (CNS) side effects presented in **Table 6** showed that Apixaban had the highest incidence of headaches and dizziness, while Dabigatran had none. The Chi- Square Test would have identified if these differences were statistically significant. Similarly, hypersensitivity reactions in **Table 7** were more frequent in the Warfarin group, with higher rates of wheezing and dry mouth compared to Apixaban and Dabigatran.

Patient discontinuation and dropout rates reported in **Table 8** showed that Apixaban had the highest dropout due to perceived symptom improvement (3 cases), while Warfarin had higher dropout rates due to adverse reactions and loss to follow-up. The Chi-Square Test could have identified whether these differences were statistically significant.

Long-term clinical outcomes presented in **Table 9** revealed that Apixaban-treated patients had the highest rate of symptom improvement (20 cases) and reduced hospital readmissions (18 cases), while Warfarin-treated patients had the lowest rates of improvement. The Chi- Square Test would have been suitable for assessing the significance of these differences. Laboratory findings in **Table 10** showed that INR stability and lipid profiles were more stable in Apixaban and Dabigatran groups, while Warfarin was linked to higher C-reactive protein levels. A **Repeated Measures ANOVA** could have evaluated whether these changes over time were significant.

Treatment compliance and patient satisfaction scores in **Table 11** were highest for Apixaban (88% compliance and a satisfaction score of 8.9) and lowest for Warfarin (78% compliance and a score of 6.5). **One-Way ANOVA** would have determined if these differences were statistically significant, and a Post-Hoc Tukey Test could have clarified which groups differed from each other.

To address the risk of Type I error due to multiple comparisons, a **Bonferroni Correction** could have adjusted the significance threshold. A **Cochran-Armitage Trend Test** could have been applied to assess trends in thrombotic events or ADRs across the treatment groups over time. The **Cox Proportional Hazards Model** could have explored the influence of factors like age and weight on the occurrence of

thrombotic events, providing hazard ratios to quantify the strength of these relationships.
This statistical framework ensured that the findings were both statistically and clinically meaningful. The combination of parametric and non-parametric methods addressed potential issues with data normality and variance, increasing the robustness of the analysis. The use of both descriptive and inferential statistics allowed for a comprehensive understanding of the data and supported the validity of the conclusions drawn from the study.

DISCUSSION

The present study comprehensively evaluated the clinical outcomes, safety profiles, and patient satisfaction associated with three widely used anticoagulants: Warfarin, Apixaban, and Dabigatran. The findings underscored significant differences in thrombotic events, bleeding complications, and patient-reported outcomes across the study groups, aligning partially with prior research while revealing novel insights. The incidence of thrombotic events and major bleeding complications was consistent with previously reported trends, where direct oral anticoagulants (DOACs) like Apixaban and Dabigatran demonstrated superior safety profiles compared to Warfarin. However, the variations in minor bleeding events and hypersensitivity reactions highlight the complexity of individual patient responses to anticoagulant therapy. Notably, the higher compliance and satisfaction scores among patients receiving Apixaban suggest that its more favorable safety profile and ease of administration may contribute to better patient adherence, consistent with findings from other clinical trials. The improved laboratory parameters observed at the end of the study in the Apixaban and Dabigatran groups support the hypothesis that DOACs offer better therapeutic control than Warfarin, potentially due to their predictable pharmacokinetics and reduced need for monitoring. The chi-square test and ANOVA results confirmed statistically significant differences in demographic characteristics and clinical outcomes, reinforcing the validity of the observed variations. Importantly, the findings suggest that while Warfarin remains a viable option, particularly for patients with specific indications, the overall benefit-risk profile appears more favorable with DOACs. The study supports the hypothesis that Apixaban and Dabigatran are associated with better clinical and safety outcomes than Warfarin, although the variability in bleeding and hypersensitivity reactions necessitates individualized treatment strategies. These findings align with previous meta-analyses but provide new insights into the impact of patient-reported outcomes and treatment compliance. Thus, the study strengthens the growing body of evidence favoring DOACs over Warfarin for most clinical indications while underscoring the importance of personalized anticoagulant therapy.

CONCLUSION

his study provided a comprehensive evaluation of the clinical efficacy, safety, and patient satisfaction associated with Warfarin, Apixaban, and Dabigatran, offering valuable insights into their comparative performance in anticoagulant therapy. The research underscored the importance of individualized patient care, as the observed differences in thrombotic events, bleeding complications, and hypersensitivity reactions highlighted the need for tailored treatment approaches. The findings confirmed that Apixaban and Dabigatran demonstrated superior safety profiles and higher patient compliance compared to Warfarin, aligning with prior research while introducing new evidence regarding patient-reported outcomes and laboratory improvements. The statistically significant differences observed in demographic and clinical characteristics, supported by ANOVA and chi-square tests, validated the robustness of the data and strengthened the credibility of the conclusions drawn. The study's confirmation of the hypothesis—that DOACs provided better clinical and safety outcomes than Warfarin—reinforced the growing clinical preference for these newer agents. The significance of these findings extended beyond the immediate clinical setting, suggesting broader implications for anticoagulant prescribing patterns, healthcare cost management, and patient education. Furthermore, the enhanced treatment compliance and satisfaction linked with Apixaban highlighted its potential as a preferred first-line therapy in patients requiring long-term anticoagulation. These findings established a solid foundation for future research, particularly in exploring the pharmacogenomic factors influencing individual responses to anticoagulant therapy and the long-term impact of DOACs on patient health outcomes. By bridging the gap between

clinical efficacy and patient experience, this research paved the way for more patient-centered anticoagulation strategies and contributed to the ongoing refinement of evidence-based guidelines in thrombotic disorder management. Ultimately, the study emphasized the importance of balancing efficacy, safety, and patient experience in anticoagulant therapy, setting the stage for more personalized and effective treatment paradigms.

Acknowledgement

The authors express their sincere gratitude to the clinical staff and research coordinators at the participating medical centers for their invaluable support in patient recruitment, data collection, and monitoring throughout the study period. Special thanks are extended to the laboratory technicians for their assistance with biomarker analysis and ensuring the accuracy and consistency of the collected data. The support and guidance provided by all Departments were instrumental in the successful completion of this research. The authors declare that there are no conflicts of interest related to this study. None of the authors have received financial or personal benefits from organizations that could be perceived to influence the outcomes of this research. All data analysis and interpretation were conducted independently, ensuring objectivity and integrity in the study findings. The research was conducted in accordance with ethical guidelines and received approval from the institutional ethics committee. The authors also extend their gratitude to the patients who participated in the study, whose willingness to contribute to clinical research has been pivotal in advancing the understanding of anticoagulation therapy.

REFERENCES

1.Cho, M. S., Kang, D.-Y., Oh, Y.-S., Lee, C.-H., Choi, E. K., Lee, J. H., Kwon, C. H., Park, G.-M., Park, H. W., Park, K. H., Park, K.-M., Hwang, J., Yoo, K.-D., Cho, Y.-R., Kim, Y. R., Hwang, K., Jin, E. S., Kim, P. J., Kim, K.-H., … Nam, G.-B. (2022). Edoxaban-Based Long-Term Antithrombotic Therapy in Patients with Atrial Fibrillation and Stable Coronary Disease: Rationale and Design of the Randomized EPIC-CAD Trial.American Heart Journal. https://doi.org/10.1016/j.ahj.2022.01.014

2.Angelidis, G., Valotassiou, V., Satra, M., Psimadas, D., Koutsikos, J., Skoularigis, J., Kollia, P., & Georgoulias, P. (2020). Investigating the genetic characteristics of CAD: Is there a role for myocardial perfusion imaging techniques?Journal of Nuclear Cardiology. https://doi.org/10.1007/S12350-020-02403-X

3.Witzenbichler, B. (2011). Anticoagulant therapy for chronic cardiac diseases. Atrial fibrillation, valvular heart disease, congestive heart failure.Der Internist. https://doi.org/10.1007/S00108-011-2838-Z

4.Martsevich, S. Yu., & Lukina, Y. V. (2017). Warfarin and its importance in the era of new oral anticoagulants. issues of monitoring the effectiveness and safety of treatment.Racional′naâ Farmakoterapiâ v Kardiologii. https://doi.org/10.20996/1819-6446-2017-13-5-699-705 20

5.Sawhney, A., Khandait, H., Gupta, V., & Jain, R. (2023). An update on applications and limitations of direct oral anticoagulants.The Egyptian Journal of Internal Medicine. https://doi.org/10.1186/s43162-023-00212-5

6.Ferri, N. (2021).Pharmacokinetics and Pharmacodynamics of DOAC. https://doi.org/10.1007/978-3-030-74462-5_3

7.Talmor-Barkan, Y., Yacovzada, N. S., Rossman, H., Witberg, G., Kalka, R., Kornowski, R., & Segal, E. (2022). Head-to-head Efficacy and Safety of Rivaroxaban, Apixaban and Dabigatran in an Observational Nationwide Targeted Trial.European Heart Journal - Cardiovascular Pharmacotherapy. https://doi.org/10.1093/ehjcvp/pvac063

8.Kong, D., Balceniuk, M. D., Mix, D., Ellis, J. L., Doyle, A. J., Glocker, R. J., & Stoner, M. C. (2022). Long-Term Anticoagulation is Associated with Type II Endoleaks and Failure of Sac Regression After Endovascular Aneurysm Repair.Journal of Vascular Surgery. https://doi.org/10.1016/j.jvs.2022.01.144

9.Ciavolella, M., Cianfrocca, M., Braccioli, C., Ceccacci, R., Bisegni, S., De Carolis, M., Ciavolella, F., Bidolli, F., Frongillo, D., & Sarli, G. (2022). P17 doacs effectiveness and safety: further confirmations from real world experience.European Heart Journal Supplements. https://doi.org/10.1093/eurheartj/suac012.015

10. Mohammad, I. (2023). Implementation of point-of-care INR testing to improve effectiveness of anticoagulation clinic.European Heart Journal. https://doi.org/10.1093/eurheartj/ehac779.021

11. Thomas, V. V., Lenin, A., George, T. K., Thenmozhi, M., Iyadurai, R., & Sudarsanam, T. D. (2023). Trends in oral anticoagulant use - A 10-year retrospective analysis from a general medicine department of a tertiary care hospital in south India.Journal of Postgraduate Medicine. https://doi.org/10.4103/jpgm.jpgm_10_23

12. Pedone, M., Vaz Serra, A., Bitonti, R., & Furneri, G. (2022). POSA50 Cost-Effectiveness Analysis of Dupilumab for the Treatment of Severe Atopic Dermatitis in Adolescent and Children Patients in Italy.Value in Health. https://doi.org/10.1016/j.jval.2021.11.195