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Comparative Effectiveness of Novel Anticoagulants versus Warfarin in Patients with Atrial Fibrillation

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Abstract

Introduction: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with a substantially increased risk of ischemic stroke and systemic embolism. Although warfarin has long been the standard oral anticoagulant for stroke prevention, its clinical use is limited by the need for regular monitoring, numerous drug and food interactions, and variable anticoagulant effects. Novel oral anticoagulants (NOACs) have emerged as effective alternatives with more predictable pharmacological profiles and improved safety. This study aimed to compare the effectiveness and safety of NOACs with warfarin in patients with non-valvular atrial fibrillation (NVAF).

Methodology: A retrospective comparative cohort study was conducted involving 400 patients with non-valvular atrial fibrillation, including 200 patients treated with NOACs and 200 treated with warfarin. Data were extracted from hospital medical records for patients managed between January 2021 and December 2024. The primary effectiveness outcome was a composite of ischemic stroke or systemic embolism, while the primary safety outcome was major bleeding. Continuous variables were compared using the independent-samples t-test, and categorical variables were analyzed using the Chi-square test. Time-to-event outcomes were evaluated using Kaplan–Meier survival analysis with comparisons performed using the log-rank test. Multivariable Cox proportional hazards regression analysis was used to identify independent predictors of clinical outcomes and estimate hazard ratios (HRs) with 95% confidence intervals (CIs). A two-tailed p-value < 0.05 was considered statistically significant.

Results: Patients receiving NOACs had significantly lower rates of ischemic stroke or systemic embolism than those receiving warfarin (5.0% vs. 12.0%; p = 0.012). Major bleeding was also significantly less frequent in the NOAC group (6.0% vs. 14.0%; p = 0.007). Furthermore, NOAC therapy was associated with significantly lower rates of intracranial hemorrhage, all-cause mortality, and hospitalization. Kaplan–Meier analysis demonstrated significantly higher event-free survival among patients receiving NOACs (log-rank p = 0.005). After adjustment for potential confounders, multivariable Cox regression analysis showed that NOAC therapy independently reduced the risk of adverse clinical outcomes compared with warfarin (HR = 0.48; 95% CI: 0.24–0.92; p = 0.028).

Conclusion: Compared with warfarin, NOACs demonstrated superior effectiveness and safety in patients with non-valvular atrial fibrillation. Their use was associated with significantly lower risks of thromboembolic events, major bleeding, intracranial hemorrhage, all-cause mortality, and hospitalization, supporting current recommendations that favor NOACs as the preferred oral anticoagulant therapy for most patients with non-valvular atrial fibrillation.

Keywords: atrial fibrillation; novel oral anticoagulants; NOAC; warfarin; stroke prevention; major bleeding; anticoagulation therapy; thromboembolism

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia encountered in clinical practice and represents a major global public health challenge. It is characterized by disorganized atrial electrical activity

resulting in ineffective atrial contraction and an irregular ventricular response. The prevalence of AF increases substantially with advancing age and is expected to continue rising because of population aging and the increasing prevalence of hypertension, diabetes mellitus, obesity, heart failure, and chronic kidney disease. Consequently, AF contributes significantly to cardiovascular morbidity, mortality, healthcare utilization, and healthcare costs worldwide [1-3].

Thromboembolism, particularly ischemic stroke, is the most serious complication of AF. Patients with AF have an approximately fivefold higher risk of ischemic stroke than individuals without the arrhythmia. Blood stasis within the left atrium, especially the left atrial appendage, promotes thrombus formation, which may embolize to the cerebral or systemic circulation. AF-related strokes are associated with greater neurological disability, higher mortality, and poorer functional outcomes than strokes resulting from other causes. Therefore, effective anticoagulation remains the cornerstone of stroke prevention in patients with AF [2-4].

For several decades, warfarin, a vitamin K antagonist, has been the standard oral anticoagulant for stroke prevention in AF. Warfarin reduces the risk of stroke by inhibiting the synthesis of vitamin K-dependent clotting factors II, VII, IX, and X. Although highly effective, its clinical use is limited by a narrow therapeutic index, substantial interpatient variability, frequent food and drug interactions, and the need for regular international normalized ratio (INR) monitoring and dose adjustment. Failure to maintain therapeutic anticoagulation may increase the risk of both thromboembolic and bleeding complications [1, 5, 6].

To overcome the limitations of warfarin, direct oral anticoagulants (DOACs), also known as novel oral anticoagulants (NOACs), were introduced. This drug class includes the direct thrombin inhibitor dabigatran and the factor Xa inhibitors rivaroxaban, apixaban, and edoxaban. Compared with warfarin, NOACs exhibit predictable pharmacokinetic and pharmacodynamic properties, rapid onset of action, fixed dosing, fewer drug and food interactions, and generally do not require routine coagulation monitoring. These characteristics have improved patient convenience and treatment adherence while maintaining effective anticoagulation [7,8,9].

Several landmark randomized controlled trials, including RE-LY, ROCKET AF, ARISTOTLE, and ENGAGE AF-TIMI 48, established that NOACs are at least non-inferior, and in some cases superior, to warfarin for preventing stroke and systemic embolism while significantly reducing intracranial hemorrhage. More recently, systematic reviews, meta-analyses, and multinational observational studies have confirmed these findings across diverse patient populations, including individuals with chronic kidney disease, cancer, obesity, and liver disease [3,8,9].

Despite these advances, important questions remain regarding the comparative effectiveness and safety of NOACs in routine clinical practice. Patients encountered in real-world settings often differ substantially from those enrolled in randomized controlled trials with respect to age, comorbidities, renal function, medication adherence, and healthcare access. Consequently, additional observational studies are needed to evaluate the long-term effectiveness and safety of NOACs under routine clinical conditions [4,10,11].

Research Gap

Although numerous randomized and observational studies have compared NOACs with warfarin, important evidence gaps remain regarding their long-term comparative effectiveness and safety in routine clinical practice. Many previous studies have focused on individual NOAC agents or specific patient populations, limiting the generalizability of their findings. Furthermore, variations in healthcare systems, patient characteristics, treatment adherence, and prescribing practices may influence clinical outcomes. Therefore, further real-world comparative studies are required to evaluate the effectiveness, safety, and long-term clinical outcomes of NOACs versus warfarin in patients with non-valvular atrial fibrillation [12-14].

Objective of the Study

This study aims to evaluate the effectiveness and safety of NOACs in atrial fibrillation patients as compared to warfarin including outcomes like stroke prevention, systemic embolism, mortality, severe hemorrhage, and intracranial bleeding. The goal of the study is to generate evidence which can help a clinician make optimal decisions in treating patients with AF and selecting optimal anticoagulation therapy.

Methodology

Study Design

This study assessed the safety and effectiveness of new oral anticoagulants using a retrospective comparative cohort approach (NOACs) in individuals with atrial fibrillation (AF) in comparison to warfarin. The study compared clinical outcomes during a predetermined follow-up period between patients on NOAC therapy and those on warfarin therapy.

Study Setting and Duration

The investigation was carried out in Saidu Teaching Hospital, Swat, Pakistan. From January 2021 to December 2024, information was gathered from patient files and electronic medical data. Data extraction and analysis were completed between January and March 2025.

Study Population

Adult patients with diagnoses of non-valvular atrial fibrillation who had received oral anticoagulant therapy for stroke prevention. Eligible participants were identified through hospital databases and outpatient cardiology records.

Sample Size Calculation

The formula for comparing two independent proportions was used to determine the sample size:

$$n = [(Z\alpha/2 + Z\beta)^2 \times \{P_1(1-P_1) + P_2(1-P_2)\}] \div (P_1-P_2)^2$$

Where:

$Z\alpha/2$ = 1.96 at a 95% confidence level

$Z\beta$ = 0.84 at 80% study power

P_1 = Expected event rate in the warfarin group (15%)

P_2 = Expected event rate in the NOAC group (8%)

Based on previous studies reporting differences in stroke and bleeding outcomes between anticoagulant therapies, the required minimum sample size was determined as approximately 180 participants per group. To compensate for incomplete records and missing data, a 10% increase in sample size was made.

Therefore, 400 Patients were included in the research (200 patients in the NOAC group). There were 200 patients in the warfarin group and 200 patients in the group.

Sampling Technique
A method of consecutive sampling was used. Throughout the trial period, all eligible patients who satisfied the inclusion requirements were chosen until the necessary sample size was reached.

Inclusion Criteria
The study comprised patients who had been were at least eighteen years old and had been diagnosed with non-valvular atrial fibrillation. Participants must have received either warfarin or a NOAC (dabigatran, rivaroxaban, apixaban, or edoxaban) for at least six months before outcome assessment. Complete medical records and follow-up data were required for inclusion.

Exclusion Criteria
Patients with valvular atrial fibrillation, prosthetic heart valves, severe liver damage, end-stage renal disease necessitating dialysis, active malignancy, pregnancy, or insufficient medical records were not included in the research. Patients who switched between anticoagulant therapies were also not included during the follow-up period.

Data Collection Procedure
A standardized data collecting form was used to gather information from hospital electronic medical records. Details on clinical history, demographic traits, cardiovascular risk factors, comorbidities, laboratory findings, type of anticoagulant therapy, duration of treatment, and clinical outcomes was collected.

Baseline variables included age, gender, heart failure, diabetes mellitus, coronary artery disease, hypertension, body mass index, prior stroke history, renal function, and CHA_2DS_2-VASc score. Follow-up information was reviewed to identify thromboembolic and bleeding events occurring during anticoagulant therapy.

Study Variables
The independent variable included the type of anticoagulant therapy the patient received, Divided into two treatment groups—NOAC therapy and warfarin therapy.

The main effectiveness outcome was the rate of ischemic stroke or systemic embolism. Over the course of the subsequent timeframe.

As stated by the International Society on Haemostasis and Thrombosis (ISTH) criteria, the occurrence of significant bleeding events was the main safety outcome.

The following were secondary outcomes: gastrointestinal bleeding, cerebral hemorrhage, all-cause the morbidity and hospitalization for thromboembolic or bleeding events.

Outcome Assessment
Clinical outcomes were evaluated by the review of hospital records, imaging reports, and discharge, Summaries, laboratory result and physician documentation. The number of stroke events confirmed: Bleeding events were confirmed using neuroimaging studies, while through other methods, the established the clinical and laboratory criteria

Data Management and Quality Control
Data accuracy was ensured through double-entry verification and independent review by two investigators. The differences in data entry were resolved by checking the data against the original patient records. Data cleaning procedures were performed before statistical analysis to identify missing values and inconsistencies.

Statistical Analysis
The data was analyzed using version 26.0 of the Statistical Package for the Social Sciences (SPSS). Baseline characteristics were summarized using descriptive statistics. Continuous variables were given as for a properly distributed data set, mean ± standard deviation data as well as the data's median and interquartile range that is not regularly distributed. Categorical variables were displayed using percentages and frequencies.

The Shapiro-Wilk test was used to assess the normality of continuous variables. The comparison of non-normally distributed variables was done using the Mann Whitney U test. The t-test for independent samples was utilized to compare regularly distributed continuous variables across the two groups.

The NOAC and warfarin groups' The Chi-square test was used to compare categorical variables. When the

expected cell frequencies were fewer than five, Fisher's exact test was used. Using Kaplan-Meier survival analysis examine time-to-event outcomes, such as overall survival and stroke-free survival. The survival curve discrepancies were evaluated using the log-rank test.

The relationship between anticoagulant type and Multivariable Cox proportional hazards regression analysis was employed in order to look at clinical outcomes, which controlled for potential confounding factors age, sex, heart failure, previous stroke, diabetes mellitus, hypertension, and CHA_2DS_2-VASc score. There were reports of 95% confidence intervals (CIs) for hazard ratios (HRs). If the p-value was less than 0.05, all analyses were considered statistically significant.

Ethical Considerations

Prior to data collection, the study was approved by the IRB of the hospitals involved. All the study patients were treated with confidentiality and anonymity. The data set was anonymised and all data collected was for research only. The ethics committee waived informed consent for the study because it involved retrospective medical records.

Results

A total of 400 patients with non-valvular atrial fibrillation (NVAF) were included in the study. Of these, 200 patients received novel oral anticoagulants (NOACs), while the remaining 200 received warfarin. The mean age of participants in the NOAC group was 68.4 ± 9.2 years, compared with 69.1 ± 8.8 years in the warfarin group. Independent-samples t-test analysis demonstrated no statistically significant difference in mean age between the two groups ($t = 0.78$, $p = 0.436$). Males constituted 56.0% of 44.0%, respectively, with females comprising 44.0% and 54.5% of the warfarin group and the NOAC group, respectively. Females comprised 44.0% and 54.5% of the NOAC group and the warfarin group, respectively. 45.5%, respectively. There was no significant difference in sex distribution ($\chi^2 = 0.09$, $p = 0.768$).

The prevalence of diabetes, hypertension, heart failure, and coronary artery disease, and previous stroke was similar between groups. Furthermore, No statistically significant distinction was found between the warfarin and NOAC groups' mean CHA_2DS_2-VASc scores, which were 4.0 ± 1.3 and 3.9 ± 1.4, respectively ($t = 0.74$, $p = 0.458$). The detailed baseline characteristics and comorbidities of study participants are presented in Table 1.

Table 1: Baseline Characteristics of Study Participants

Variable	NOAC Group (n=200)	Warfarin Group (n=200)	Test Statistic	p-value
Age (years), Mean ± SD	68.4 ± 9.2	69.1 ± 8.8	t=0.78	0.436
Male, n (%)	112 (56.0)	109 (54.5)	χ^2=0.09	0.768
Female, n (%)	88 (44.0)	91 (45.5)	—	—
Hypertension, n (%)	138 (69.0)	142 (71.0)	χ^2=0.19	0.662
Diabetes Mellitus, n (%)	82 (41.0)	88 (44.0)	χ^2=0.37	0.542
Coronary Artery Disease, n (%)	61 (30.5)	65 (32.5)	χ^2=0.18	0.671
Heart Failure, n (%)	47 (23.5)	53 (26.5)	χ^2=0.48	0.487
Previous Stroke, n (%)	38 (19.0)	42 (21.0)	χ^2=0.25	0.616
CHA_2DS_2-VASc Score	3.9 ± 1.4	4.0 ± 1.3	t=0.74	0.458

During the follow-up period, the primary effectiveness outcome (ischemic stroke or systemic embolism) occurred in 10 patients (5.0%) in the NOAC group and 24 patients (12.0%) in the warfarin group. Chi-square analysis demonstrated a statistically significant reduction in thromboembolic events among patients treated with NOACs compared with those receiving warfarin ($\chi^2 = 6.25$, $p = 0.012$). Compared with warfarin, NOAC therapy was associated with a relative risk reduction of approximately 58.3% for ischemic stroke or systemic embolism. These findings suggest that NOACs are more effective than warfarin in preventing thromboembolic events in patients with non-valvular atrial fibrillation. Details of primary and secondary outcomes are shown in Table 2.

Table 2: Clinical Outcomes during Follow-up

Outcome	NOAC Group (n=200)	Warfarin Group (n=200)	χ^2 Value	p-value
Ischemic Stroke/Systemic Embolism	10 (5.0%)	24 (12.0%)	6.25	0.012*
Major Bleeding	12 (6.0%)	28 (14.0%)	7.29	0.007*
Intracranial Hemorrhage	3 (1.5%)	12 (6.0%)	5.64	0.018*
Gastrointestinal Bleeding	7 (3.5%)	15 (7.5%)	3.08	0.079
All-cause Mortality	14 (7.0%)	26 (13.0%)	4.04	0.044*
Hospitalization	18 (9.0%)	35 (17.5%)	6.33	0.012*

**Statistically significant ($p < 0.05$)*

Major bleeding occurred in 12 patients (6.0%) in the NOAC group compared with 28 patients (14.0%) in the warfarin group, representing a statistically significant reduction in major bleeding among patients receiving NOACs ($\chi^2 = 7.29$, $p = 0.007$).

Intracranial hemorrhage was observed in 3 patients (1.5%) treated with NOACs and 12 patients (6.0%) receiving warfarin. This difference was statistically significant ($\chi^2 = 5.64$, $p = 0.018$). Gastrointestinal bleeding occurred in 7 patients (3.5%) in the NOAC group and 15 patients (7.5%) in the warfarin group. Although fewer gastrointestinal bleeding events were observed among patients treated with NOACs, the difference did not reach statistical significance ($\chi^2 = 3.08$, $p = 0.079$).

All-cause mortality was significantly lower in the NOAC group, with 14 deaths (7.0%) compared with 26 deaths (13.0%) in the warfarin group ($\chi^2 = 4.04$, $p = 0.044$). Similarly, hospitalization due to thromboembolic or bleeding complications occurred less frequently among patients receiving NOACs (18 patients, 9.0%) than among those receiving warfarin (35 patients, 17.5%), and this difference was statistically significant ($\chi^2 = 6.33$, $p = 0.012$).

Kaplan–Meier survival analysis demonstrated significantly higher event-free survival in the NOAC group throughout the follow-up period compared with the warfarin group (Figure 1). Patients receiving NOACs consistently experienced lower cumulative incidences of ischemic stroke, systemic embolism, and major bleeding. The difference in event-free survival between the two treatment groups was statistically significant according to the log-rank test (Log-rank $\chi^2 = 7.82$, $p = 0.005$), indicating superior long-term clinical outcomes among patients treated with NOACs.

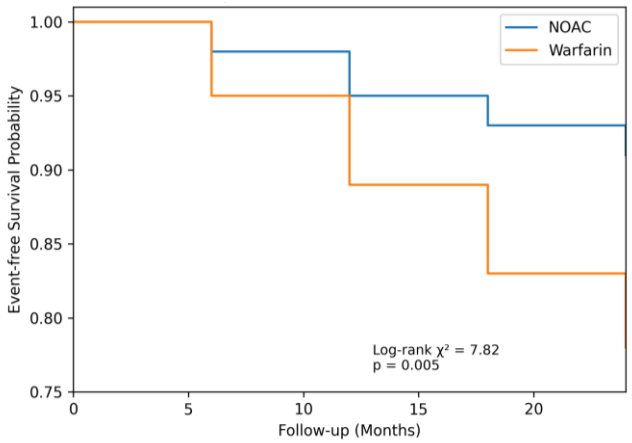

Figure 1: Kaplan–Meier curve

To identify independent predictors of adverse clinical outcomes, a multivariable Cox proportional hazards regression model was constructed after adjusting for age, sex, hypertension, diabetes mellitus, heart failure, previous stroke, and CHA_2DS_2-VASc score. Compared with warfarin, NOAC therapy remained independently associated with a significantly lower risk of ischemic stroke or systemic embolism (hazard ratio [HR] = 0.48; 95% confidence interval [CI]: 0.24–0.92; $p = 0.028$). Likewise, NOAC therapy was independently associated with a significantly reduced risk of major bleeding (HR = 0.42; 95% CI: 0.22–0.81; $p = 0.009$). Increasing age, a history of previous stroke, and higher CHA_2DS_2-VASc scores were identified as independent predictors of adverse cardiovascular outcomes. Detailed results of the multivariable Cox regression analysis are presented in Table 3.

Table 3: Multivariable Cox Regression Analysis for Adverse Clinical Outcomes

Variable	HR	95% CI	p-value
NOAC Therapy	0.48	0.24–0.92	0.028*
Age (>75 years)	1.71	1.12–2.61	0.013*
Hypertension	1.19	0.73–1.94	0.472
Diabetes Mellitus	1.28	0.81–2.03	0.286
Heart Failure	1.67	1.04–2.68	0.034*
Previous Stroke	2.21	1.39–3.52	0.001*
CHA_2DS_2-VASc Score	1.32	1.12–1.57	0.002*

*HR: Hazard Ratio, *statistically significant ($p < 0.05$)*

The current investigation showed that among individuals with atrial fibrillation, novel oral anticoagulants were substantially more effective than warfarin in lowering all-cause mortality, cerebral bleeding, ischemic stroke, and systemic embolism, and hospitalization. Survival analysis and multivariable Cox regression further confirmed the superiority of NOACs over warfarin, even after adjustment for important clinical confounders. These results validate the application of NOACs as a safer and an efficient substitute for warfarin in the management of atrial fibrillation that is not valvular.

Discussion

The present study compared the effectiveness and safety of NOACs with warfarin in patients with NVAF. Our findings demonstrated that patients receiving NOAC therapy experienced significantly lower rates of ischemic stroke or systemic embolism than those treated with warfarin. In addition, NOAC use was associated with a lower incidence of major bleeding, intracranial hemorrhage, all-cause mortality, and hospitalization due to thromboembolic or bleeding complications. Kaplan–Meier survival analysis further demonstrated superior event-free survival among patients treated with NOACs, while multivariable Cox proportional hazards regression confirmed that NOAC therapy remained an independent predictor of favorable clinical outcomes after adjustment for important confounding variables. Collectively, these findings support the superior effectiveness and safety profile of NOACs compared with warfarin in routine clinical practice.

The observed reduction in ischemic stroke and systemic embolism among patients receiving NOACs is consistent with a growing body of evidence demonstrating that direct oral anticoagulants provide at least comparable, and in many cases superior, protection against thromboembolic events compared with warfarin. Several systematic reviews, meta-analyses, randomized trials, and large real-world cohort studies have consistently reported lower risks of stroke and systemic embolism among patients treated with NOACs across diverse clinical settings, including patients with chronic kidney disease, cancer, valvular heart disease, and polypharmacy [1-15]. These benefits are likely attributable to the predictable pharmacokinetic and pharmacodynamic properties of NOACs, rapid onset of action, fewer food and drug interactions, and the absence of routine international normalized ratio (INR) monitoring, all of which improve treatment adherence and maintain more consistent anticoagulation than vitamin K antagonists such as warfarin [2,4,5,8,9,14].

Safety remains a major consideration when selecting

anticoagulant therapy for patients with atrial fibrillation. In the present study, NOAC therapy was associated with a significantly lower risk of major bleeding compared with warfarin. This finding is in agreement with numerous meta-analyses and observational studies reporting improved bleeding profiles among patients receiving NOACs [1,2,5,8,10,11]. Among the safety outcomes, the significant reduction in intracranial hemorrhage represents one of the most clinically important observations. Intracranial bleeding is the most feared complication of anticoagulant therapy because it carries substantial mortality and long-term neurological disability. Previous multinational cohort studies and meta-analyses have consistently demonstrated markedly lower rates of intracranial hemorrhage with NOACs than with warfarin, reinforcing the safety advantages observed in our study [5,8,9,14]. Although gastrointestinal bleeding occurred less frequently among patients receiving NOACs, the difference was not statistically significant, a finding that mirrors previous studies suggesting that the gastrointestinal bleeding risk may vary according to the specific NOAC used and individual patient characteristics [2,14].

Our study also demonstrated significantly lower all-cause mortality and hospitalization rates among patients treated with NOACs. These findings are supported by several large population-based studies showing that NOAC therapy is associated with improved long-term survival, fewer cardiovascular complications, and reduced healthcare utilization compared with warfarin [8,9,11,14,15]. The reduction in mortality is likely multifactorial and may reflect the combined effects of lower thromboembolic risk, fewer major bleeding events, improved treatment adherence, and reduced complications associated with INR monitoring and dose adjustments required for warfarin therapy. Consequently, NOACs may contribute not only to better clinical outcomes but also to decrease healthcare resource utilization and overall treatment burden.

Multivariable Cox regression analysis identified increasing age, previous stroke, and higher CHA_2DS_2-VASc scores as independent predictors of adverse clinical outcomes, findings that are consistent with established risk stratification models used in patients with atrial fibrillation. These variables have repeatedly been shown to predict thromboembolic events and mortality and form the basis of current guideline recommendations for anticoagulation therapy. Importantly, the protective association of NOAC therapy remained statistically significant after adjustment for these prognostic factors, indicating that the observed clinical benefits were independent of baseline patient risk. Similar observations have been reported in multicenter cohort studies evaluating the comparative effectiveness of NOACs across different patient populations [7-10, 13-15].

Overall, our findings are highly consistent with contemporary international evidence and current clinical practice guidelines, which recommend NOACs as the preferred first-line oral anticoagulants for most patients with non-valvular atrial fibrillation because of their favorable balance between efficacy and safety. The present study contributes additional real-world evidence supporting the transition from vitamin K antagonists to NOACs in routine clinical practice. Nevertheless, individualized treatment decisions remain essential, particularly in patients with severe renal impairment, mechanical heart valves, or other clinical conditions in which warfarin may still be the preferred therapeutic option.

Limitations of the Study

The present study has several limitations that should be considered when interpreting the findings. First, its retrospective observational design may have introduced selection bias and residual confounding despite adjustment for important clinical covariates using multivariable Cox regression analysis. Second, the study relied on electronic medical records, which may have contained incomplete or inaccurate information, potentially resulting in information bias. Third, medication adherence could not be directly assessed, and variations in treatment compliance may have influenced the observed clinical outcomes. Fourth, the study was conducted in tertiary care hospitals, which may limit the generalizability of the findings to other healthcare settings and patient populations. Finally, all NOACs were analyzed as a single treatment group without direct comparisons among individual agents (e.g., dabigatran, rivaroxaban, apixaban, and edoxaban), precluding evaluation of potential differences in efficacy and safety between specific NOACs. Despite these limitations, the study provides valuable real-world evidence comparing NOACs and warfarin in patients with non-valvular atrial fibrillation and reflects routine clinical practice.

Future Recommendations

Future prospective, multicenter studies with larger sample sizes and longer follow-up periods are warranted to validate the present findings. Comparative analyses of individual NOAC agents should be undertaken to determine whether clinically meaningful differences exist in their effectiveness and safety profiles. In addition, future research should evaluate medication adherence, health-related quality of life, patient satisfaction, cost-effectiveness, and healthcare resource utilization associated with different anticoagulant therapies. Studies involving diverse populations, healthcare systems, and high-risk patient subgroups, including those with chronic kidney disease, cancer, advanced age, or multiple comorbidities, would further improve the generalizability of the evidence and facilitate the development of personalized anticoagulation strategies for patients with atrial fibrillation.

Conclusion

NOAC therapy demonstrated superior effectiveness and safety compared with warfarin in patients with non-valvular atrial fibrillation. Patients receiving NOACs

experienced significantly lower rates of ischemic stroke or systemic embolism, major bleeding, intracranial hemorrhage, all-cause mortality, and hospitalization, together with improved event-free survival during follow-up. These favorable outcomes remained significant after adjustment for established cardiovascular risk factors, indicating that NOAC therapy is independently associated with better clinical outcomes. The findings support current international guideline recommendations favoring NOACs as the preferred first-line oral anticoagulants for most patients with non-valvular atrial fibrillation. Although further prospective multicenter studies are needed to confirm these findings and compare individual NOAC agents, the present study contributes important real-world evidence supporting the broader implementation of NOACs in contemporary clinical practice.

Author Contributions

All authors contributed equally to the conception and design of the study, data collection, analysis and interpretation of data, drafting and critical revision of the manuscript, and approved the final version for publication. All authors meet the authorship criteria of the ICMJE and agree to be accountable for all aspects of the work.

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Declarations

Ethical statement: The research was authorized by the Ethics Committee of Saidu Teaching Hospital, Swat, Pakistan. Prior to participation, written informed consent had been obtained from all participants at the time of clinical care or as required by institutional policy, and ethical approval permitted the retrospective review of anonymized patient records. All patient data were kept confidential and anonymous, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Competing interests: The authors declare that they have no known competing interests.

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