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Original Research

Comparing the Efficacy of Direct Oral Anticoagulants Versus Warfarin in the Prevention of Stroke in Atrial Fibrillation Patients

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ABSTRACT:

Aim: This study aimed to compare the efficacy and safety of direct oral anticoagulants (DOACs) versus warfarin in preventing stroke and systemic embolism in patients with atrial fibrillation (AF). **Material and Methods:** This retrospective cohort study included 100 patients with non-valvular atrial fibrillation, divided into two groups: 50 receiving DOACs and 50 receiving warfarin. Baseline clinical and demographic data were collected, including age, gender, comorbidities, CHA_2DS_2-VASc, and HAS-BLED scores. Patients were followed for 12 months, and clinical outcomes, including ischemic stroke, systemic embolism, and major bleeding events, were recorded. Statistical analyses compared outcomes between groups, with significance set at $p < 0.05$. **Results:** The incidence of ischemic stroke was lower in the DOACs group (4%) compared to the warfarin group (8%), though not statistically significant ($p = 0.38$). Major bleeding events were observed in 6% of DOACs patients and 12% of warfarin patients ($p = 0.15$). Kaplan-Meier analysis showed a stroke-free survival rate of 96% for DOACs versus 92% for warfarin ($p = 0.09$). Multivariate analysis revealed that age, CHA_2DS_2-VASc, and HAS-BLED scores significantly predicted stroke risk, while DOACs were associated with a lower, non-significant hazard ratio for stroke compared to warfarin (HR: 0.72; $p = 0.32$). **Conclusion:** DOACs showed a trend toward better efficacy and safety compared to warfarin in stroke prevention and reduced bleeding risks, although differences were not statistically significant. Further large-scale studies are needed to confirm these findings and guide anticoagulation management in atrial fibrillation patients.

Keywords: Atrial fibrillation, direct oral anticoagulants, warfarin, stroke prevention, anticoagulation therapy.

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INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia, characterized by an irregular and often rapid heart rate. It significantly increases the risk of thromboembolic events, particularly ischemic stroke, which is one of the most debilitating complications associated with this condition. The lifetime risk of developing atrial fibrillation increases with age and is further influenced by various comorbidities such as hypertension, diabetes, and heart failure. Given the high prevalence of atrial fibrillation and its associated morbidity and mortality, effective anticoagulation therapy to prevent stroke is a cornerstone of clinical management.[1]The pathophysiology of stroke in atrial fibrillation is primarily related to stasis of blood in the atria, especially the left atrial appendage, which promotes thrombus formation. These clots can dislodge, leading to systemic embolism, particularly in the cerebral circulation, causing ischemic strokes. As such, anticoagulant therapy is crucial in reducing this risk by targeting the clotting cascade and minimizing thrombus formation.[2]Historically, vitamin K antagonists (VKAs), such as warfarin, have been the mainstay of anticoagulation therapy in patients with atrial fibrillation. Warfarin effectively reduces the risk of stroke by inhibiting the synthesis of vitamin K-dependent clotting factors, thereby disrupting the coagulation pathway. However, its use is associated with several limitations, including a narrow therapeutic index, the need for regular monitoring of the international normalized ratio (INR), numerous drug and food interactions, and a higher risk of bleeding complications. These challenges have prompted the development of newer anticoagulant therapies.[3]Direct oral anticoagulants (DOACs), which include agents such as dabigatran,

rivaroxaban, apixaban, and edoxaban, have emerged as effective alternatives to warfarin. Unlike warfarin, DOACs target specific components of the coagulation cascade, such as thrombin (factor IIa) or factor Xa, offering a more predictable anticoagulant effect. They have a rapid onset of action, shorter half-lives, and fewer interactions with other drugs and foods. Furthermore, DOACs eliminate the need for routine laboratory monitoring, improving convenience and adherence for patients.The introduction of DOACs has revolutionized the landscape of anticoagulation therapy in atrial fibrillation. Numerous clinical trials have demonstrated their efficacy in reducing the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation. These studies have also highlighted the potential safety advantages of DOACs, particularly in reducing the risk of major bleeding complications, including intracranial hemorrhage, which is a significant concern with warfarin therapy.[4]Despite these advancements, the choice between DOACs and warfarin is influenced by multiple factors, including patient-specific characteristics, renal function, cost, and the availability of reversal agents for bleeding events. While DOACs offer several advantages, they are not universally appropriate for all patients. For example, patients with severe renal impairment, valvular atrial fibrillation, or mechanical heart valves are typically not candidates for DOAC therapy and may require warfarin instead. Additionally, the higher cost of DOACs compared to warfarin may be a barrier to their widespread use, particularly in resource-limited settings.[5]The debate over the relative efficacy and safety of DOACs versus warfarin continues, with various studies and meta-analyses contributing to the growing body of evidence. Some studies suggest that DOACs are non-inferior or even superior to warfarin in preventing stroke and systemic embolism, while others emphasize their safety profile, particularly in reducing the risk of intracranial bleeding. However, differences in study populations, trial designs, and outcome measures have led to some variability in findings, necessitating further research to clarify these differences.[6]Another important consideration is the role of anticoagulation in high-risk subgroups, such as elderly patients, those with multiple comorbidities, or patients with prior bleeding events. These populations are often underrepresented in clinical trials but are frequently encountered in clinical practice. Understanding the relative benefits and risks of DOACs versus warfarin in these subgroups is critical for personalized decision-making and optimizing outcomes.The real-world effectiveness of DOACs compared to warfarin is another area of ongoing investigation. While clinical trials provide robust evidence, they are conducted in controlled environments with strict inclusion and exclusion criteria. Real-world studies, on the other hand, reflect the broader patient population encountered in clinical practice, including those with comorbidities, polypharmacy, and variable adherence to treatment. These studies are essential for validating the generalizability of trial findings and providing insights into the practical application of anticoagulant therapy.[7]Furthermore, the management of anticoagulation therapy in atrial fibrillation requires a multidisciplinary approach involving cardiologists, primary care physicians, pharmacists, and other healthcare providers. Patient education and shared decision-making are critical components of this process, ensuring that patients are fully informed about the benefits and risks of their treatment options. The development of anticoagulation clinics and the integration of decision-support tools can also enhance the quality of care and improve outcomes. Anticoagulation therapy remains a cornerstone in the prevention of stroke in atrial fibrillation patients. While warfarin has long been the standard of care, the advent of DOACs has transformed the management of anticoagulation, offering a more convenient and potentially safer alternative. This study aims to compare the efficacy and safety of DOACs versus warfarin in preventing stroke in atrial fibrillation patients, contributing to the ongoing discussion on optimizing anticoagulation therapy for this high-risk population.

MATERIAL AND METHODS

In this retrospective cohort study, we evaluated the efficacy of direct oral anticoagulants (DOACs) compared to warfarin in preventing stroke among patients with atrial fibrillation (AF). A total of 100 patients diagnosed with non-valvular atrial fibrillation were enrolled, with 50 patients receiving DOACs and 50 receiving warfarin as part of their anticoagulation therapy. Patients were selected from a single tertiary care hospital over a two-year period, and inclusion criteria were patients aged 18 years or older with a confirmed diagnosis of atrial fibrillation who had been prescribed anticoagulants for at least six months. Exclusion criteria included patients with valvular atrial fibrillation, a history of significant bleeding disorders, severe renal or hepatic impairment, or those with incomplete medical records.

Baseline clinical and demographic data were collected, including age, gender, body mass index (BMI), comorbid conditions (e.g., hypertension, diabetes, and heart failure), and prior history of thromboembolism or bleeding events. Stroke risk was assessed using the CHA_2DS_2-VASc score, and bleeding risk was evaluated using the HAS-BLED score. Patients were followed for a period of 12 months, during which clinical outcomes, including the incidence of ischemic stroke, systemic embolism, and major bleeding events, were recorded. The primary outcome was the occurrence of ischemic stroke, while secondary outcomes included systemic embolism and major bleeding events. Data were obtained from electronic medical records and verified by reviewing patient charts.

Statistical analysis was performed using appropriate tests to compare baseline characteristics and clinical outcomes between the two groups. Continuous variables were analyzed using the Student's t-test or Mann-Whitney U test, while categorical variables were analyzed using the chi-square test or Fisher's exact test. Kaplan-Meier survival curves were constructed to evaluate the time to the first stroke event, and Cox proportional hazards regression analysis was used to adjust for potential confounding variables. A p-value of <0.05 was considered statistically significant. This study was conducted in compliance with the Declaration of Helsinki and approved by the institutional review board, with patient confidentiality maintained throughout the research process.

RESULT

Table 1: Baseline Characteristics of Patients

The baseline characteristics of the patients in the DOACs and warfarin groups were well balanced, with no statistically significant differences between the groups (all p-values > 0.05). The average age was slightly lower in the DOACs group (70.4 ± 8.2 years) compared to the warfarin group (71.2 ± 7.9 years), but this difference was not significant (p = 0.58). The gender distribution was similar, with males constituting 56% in the DOACs group and 60% in the warfarin group (p = 0.75). The mean body mass index (BMI) was comparable between the groups (28.1 ± 3.4 vs. 27.9 ± 3.6; p = 0.68).

The prevalence of comorbid conditions such as hypertension, diabetes, and heart failure was also similar between the groups, with no significant differences. Hypertension was present in 78% of patients in the DOACs group and 82% in the warfarin group (p = 0.62), while diabetes was observed in 36% and 38% of patients, respectively (p = 0.82). Heart failure affected 22% in the DOACs group and 24% in the warfarin group (p = 0.78). Prior thromboembolism was slightly less frequent in the DOACs group (14% vs. 18%), but the difference was not significant (p = 0.45). Both groups had similar mean CHA_2DS_2-VASc (3.8 vs. 3.7; p = 0.54) and HAS-BLED scores (2.2 vs. 2.3; p = 0.49), indicating equivalent baseline stroke and bleeding risks.

Table 2: Incidence of Primary and Secondary Outcomes

The incidence of ischemic stroke was lower in the DOACs group (2 cases, 4%) compared to the warfarin group (4 cases, 8%), but this difference was not statistically significant (p = 0.38). Similarly, systemic embolism was less frequent in the DOACs group (1 case, 2%) than in the warfarin group (3 cases, 6%), with no significant difference (p = 0.28). Major bleeding events were observed in 3 patients (6%) in the DOACs group compared to 6 patients (12%) in the warfarin group, but the difference was not statistically significant (p = 0.15). Overall, the DOACs group showed a trend toward better outcomes for both efficacy (stroke prevention) and safety (reduced bleeding events), but these differences did not reach statistical significance in this cohort.

Table 3: Kaplan-Meier Analysis for Stroke

The median time to the first ischemic stroke was slightly longer in the DOACs group (11.8 months) compared to the warfarin group (10.6 months), but this difference was not significant (p = 0.21). Cumulative stroke-free survival at 12 months was 96% in the DOACs group compared to 92% in the warfarin group, with a p-value of 0.09, suggesting a non-significant trend toward improved stroke prevention in the DOACs group.

Table 4: Multivariate Cox Regression Analysis for Ischemic Stroke Risk

Multivariate Cox regression analysis demonstrated that DOACs were associated with a lower hazard ratio (HR) for ischemic stroke compared to warfarin (HR: 0.72; 95% CI: 0.38–1.37), but this was not statistically significant (p = 0.32). Age was a significant predictor of stroke risk, with each additional year increasing the hazard by 5% (HR: 1.05; 95% CI: 1.01–1.09; p = 0.04). Similarly, the CHA_2DS_2-VASc score was a strong independent predictor of stroke risk, with an HR of 1.12 (95% CI: 1.04–1.20; p = 0.01). The HAS-BLED score was also significantly associated with stroke risk (HR: 1.08; 95% CI: 1.01–1.16; p = 0.03), indicating that higher bleeding risk scores were linked to a greater likelihood of stroke.

Table 5: Safety Outcomes Comparison

The DOACs group had fewer safety events compared to the warfarin group. Intracranial hemorrhage occurred in 1 patient (2%) in the DOACs group compared to 3 patients (6%) in the warfarin group, but this difference was not statistically significant (p = 0.18). Gastrointestinal bleeding was less frequent in the DOACs group (2 cases, 4%) compared to the warfarin group (4 cases, 8%; p = 0.26). Minor bleeding events were also lower in the DOACs group (6 cases, 12%) compared to the warfarin group (9 cases, 18%; p = 0.32). Although none of these differences reached statistical significance, the results suggest a trend toward better safety outcomes with DOACs.

Table 1: Baseline Characteristics of Patients

Characteristic	DOACs Group (n=50)	Warfarin Group (n=50)	p-value
Age (mean ± SD)	70.4 ± 8.2	71.2 ± 7.9	0.58
Gender (Male/Female)	28 (56%)/22 (44%)	30 (60%)/20 (40%)	0.75
BMI (mean ± SD)	28.1 ± 3.4	27.9 ± 3.6	0.68

Hypertension	39 (78%)	41 (82%)	0.62
Diabetes	18 (36%)	19 (38%)	0.82
Heart Failure	11 (22%)	12 (24%)	0.78
Prior Thromboembolism	7 (14%)	9 (18%)	0.45
CHA_2DS_2-VASc Score (mean ± SD)	3.8 ± 1.2	3.7 ± 1.1	0.54
HAS-BLED Score (mean ± SD)	2.2 ± 0.7	2.3 ± 0.6	0.49

Table 2: Incidence of Primary and Secondary Outcomes

Outcome	DOACs Group (n=50)	Warfarin Group (n=50)	p-value
Ischemic Stroke	2 (4%)	4 (8%)	0.38
Systemic Embolism	1 (2%)	3 (6%)	0.28
Major Bleeding Events	3 (6%)	6 (12%)	0.15

Table 3: Kaplan-Meier Analysis for Stroke

Outcome	DOACs Group (n=50)	Warfarin Group (n=50)	p-value
Median Time to Stroke (months)	11.8	10.6	0.21
Cumulative Stroke-Free Survival	48 (96%)	46 (92%)	0.09

Table 4: Multivariate Cox Regression Analysis for Ischemic Stroke Risk

Variable	Hazard Ratio (HR)	95% CI	p-value
DOACs vs. Warfarin	0.72	0.38-1.37	0.32
Age	1.05	1.01-1.09	0.04
CHA_2DS_2-VASc Score	1.12	1.04-1.20	0.01
HAS-BLED Score	1.08	1.01-1.16	0.03

Table 5: Safety Outcomes Comparison

Safety Outcome	DOACs Group (n=50)	Warfarin Group (n=50)	p-value
Intracranial Hemorrhage	1 (2%)	3 (6%)	0.18
Gastrointestinal Bleeding	2 (4%)	4 (8%)	0.26
Minor Bleeding Events	6 (12%)	9 (18%)	0.32

DISCUSSION

The baseline characteristics of the study population showed no significant differences between the DOACs and warfarin groups, indicating that the cohorts were well-matched. This finding aligns with previous studies, such as Granger et al. (2011), who also demonstrated balanced baseline characteristics when comparing DOACs to warfarin in patients with atrial fibrillation. Comparable demographics and clinical parameters strengthen the validity of our findings by reducing potential confounding factors that might affect clinical outcomes.[8]The lower incidence of ischemic stroke in the DOACs group (4%) compared to the warfarin group (8%) is consistent with the findings of Connolly et al. (2009), who reported superior efficacy of DOACs (dabigatran) in reducing stroke risk. Although our results did not achieve statistical significance, likely due to the smaller sample size, they support the evidence that DOACs are effective in stroke prevention in atrial fibrillation patients. Connolly's study demonstrated that DOACs have a consistent advantage over warfarin, particularly in preventing embolic events, which is reflected in our trend-level findings.[9] The Kaplan-Meier analysis in our study revealed a trend toward better stroke-free survival in the DOACs group (96% at 12 months) compared to the warfarin group (92%). Patel et al. (2011) similarly observed improved stroke-free survival with rivaroxaban compared to warfarin in the ROCKET AF trial. These results underline the clinical benefit of DOACs, particularly in maintaining long-term stroke prevention, even if the differences are not statistically significant in smaller studies like ours.[10]Multivariate Cox regression analysis showed that age, CHA_2DS_2-VASc, and HAS-BLED scores were significant predictors of stroke risk. Our findings align with Apostolakis et al. (2012), who identified these parameters as critical in stratifying stroke and bleeding risks in atrial fibrillation patients. The slightly lower hazard ratio for DOACs compared to warfarin in our analysis (HR: 0.72) supports the growing body of evidence favoring DOACs for patients at high stroke risk.[11] In terms of safety, our study indicated fewer major bleeding events, including intracranial and gastrointestinal bleeding, in the DOACs group compared to warfarin. These findings are supported by the study by Giugliano et al. (2013), which reported significantly lower rates of intracranial hemorrhage with edoxaban compared to warfarin. Although our study's smaller sample size limits definitive conclusions, the observed trend suggests a safer bleeding profile for DOACs, consistent with large-scale trials.[12]

CONCLUSION

In conclusion, this study highlights the potential advantages of direct oral anticoagulants (DOACs) over warfarin in preventing stroke and systemic embolism in patients with atrial fibrillation, with trends suggesting improved safety profiles and fewer bleeding events. While DOACs demonstrated a numerically lower incidence of ischemic strokes and major bleeding compared to warfarin, the differences were not statistically significant, likely due to the small sample size. These findings align with existing evidence supporting the efficacy and safety of DOACs, but further large-scale studies are needed to confirm these results and guide personalized anticoagulation therapy in diverse patient populations.

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