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Comparative evaluation of the safety and efficacy of direct oral anticoagulants (DOACs) Vs. warfarin in elderly patients with atrial fibrillation

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ABSTRACT:

Background: Atrial fibrillation (AF) is a common heart rhythm disorder, particularly in the elderly population, it substantially raises the risks of a thromboembolic event, like stroke. Anticoagulation therapy is critical in the mitigation of this danger. The standard solution has been warfarin, but now direct oral anticoagulants (DOACs) have become alternatives: their potential benefits might include safety and efficacy. A comparative analysis of performance of these agents in old age groups is a vital research concern.

Objective: The aim of the study was to conduct a relative analysis on the safety and effectiveness of DOACs against warfarin among the older patient population diagnosed with atrial fibrillation.

Methods: This was a prospective observational study that was conducted in the Pakistan Institute of Medical Sciences (PIMS), Islamabad between June 2024 and May, 2025. One hundred and twenty elderly patients (age 65, years and above) with a confirmed non-valvular atrial fibrillation were recruited. Patients were relegated into two groups whereby one group was administered DOACs (apixaban, rivaroxaban or dabigatran) and another group that was given warfarin. The main assessed outcomes were placebo-substituted thromboembolic incident (stroke/systemic embolism) and significant bleeding events. There were secondary outcomes such as bleeding minor and mortality due to all causes. Information was measured after a 12-month follow-up and computed by relevant statistics.

Results: One hundred and twenty participants were randomly assigned generally with 62 participants taking DOACs and 58 taking warfarin. The rate of embolism was very low in the DOAC group (4.8) than the warfarin group (10.3) with very thin difference. Excessive bleedings were witnessed in 6.4 percent of patients on DOACs compared to 13.8 percent on warfarin. The rates of minor bleeding were also reduced in the DOAC group (11.3 percent) as opposed to the warfarin group (19.0 percent). The prevalence of all-

cause mortality was 6.4 percent in the DOAC and 8.6 percent in the warfarin groups. The results obtained on safety and efficacy between the two groups proved to be statistically significant ($p < 0.05$).
Conclusion: Compared to warfarin, DOACs showed great safety and efficacy profile in elderly patients with atrial fibrillation. The given findings confirm the preference of the DOAC treatment to warfarin among the population due to the decreases risks of the thromboembolic and bleeding events. It is suggested that more comprehensive studies be conducted to confirm the findings in some different groups of patients.
Keywords: Atrial fibrillation, direct oral anticoagulants, warfarin, elderly patients, thromboembolism, bleeding risk, anticoagulation therapy.

INTRODUCTION:

Atrial fibrillation (AF) had been identified to be the most common sustained cardiovascular malfunction, which is very common among the aging groups. It raised much more the possibility of thromboembolic events more often ischemic stroke, hence making long term anti coagulation therapy as stroke preventive therapy necessary. Historically, warfarin, a vitamin K antagonist, had been used as the standard of anticoagulation treatment with such patients [1]. Nonetheless, warfarin demanded regular testing of international normalized ratio (INR), was of narrow therapeutic range, and had many food and drugs interactions, which made it a hard management tool, particularly in elderly patients who tended to have many comorbid conditions and were on numerous drugs.

Direct oral anticoagulants (DOACs) such as apixaban, rivaroxaban, dabigatran and edoxaban had in the last decade become alternatives to warfarin [2]. These agents had a fixed dosing regime, less dietary restrictions, and less frequent labs monitoring. A number of large randomized comparative trials (RCTs), such as RE-LY, ROCKET-AF, ARISTOTLE, and ENGAGE AF-TIMI 48, were conducted to show that DOACs are non inferior or even superior to warfarin in the prevention and reduction of the stroke and the occurrence of major bleeding events. As a result of these findings, there was an enhanced use of DOACs in clinical practice, particularly in the developed countries [3]. Nevertheless, the use of DOACs had been rising with their efficiency in geriatric communities continuing to be of a significant interest to study, due to changes in drug pharmacokinetics, greater tendency to intricate bleeding, and tendency to renal systems dysfunction in this population group.

The old population; those aged 65 years and above, was the largest proportion of the AF patients with an increased risk of developing both the thromboembolic complications and anticoagulant incurred bleeding. Such two-fold susceptibility required a close calculus in the trade in safety versus efficacy in the choice of an anticoagulant [4]. The clinical use of the drug warfarin over a longer period of time had afforded physicians with comfort and control due to INR monitoring. Nonetheless, due to its complicated management, it has been that under management it causes poor compliance and unsatisfactory anticoagulation control among the elderly. More in contrast, although DOACs made treatment easy, the matters of their prolonged safety demographics among physically unstable older people and the unavailability of routine monitoring instruments was the matter of further consideration.

It was therefore necessary to have a comparative analysis of the safety and efficacy of DOACs versus warfarin in the aged patients with atrial fibrillation that could help advise evidence based clinical decision making [5]. Previously-conducted studies based on observations and analyzing real-life experience reported divergent outcomes, with some demonstrating better safety profiles of DOACs and others causing concerns with a possible risk of developing adverse effects, especially gastrointestinal bleeding or deterioration of renal functions. Moreover, cost-effectiveness, patient compliance, and comorbidities within individuals were dominant factors in making therapeutic decisions, particularly in the settings that had limited resources [6].

The rationale of this study was that those were the first safe and sound results of a study that directly and systematically compared the safety outcomes, the major anomaly being bleeding, safety outcomes, and efficacy outcomes which primarily were prevention of ischemic stroke and systemic embolism between

DOACs and warfarin in patients events in patients who are elderly having been diagnosed with atrial fibrillation. Assessing the development part of these parameters, the research has tried to offer in depth understanding of clinical advantages and limitations of the two types of anticoagulants within a susceptible age group of patients [7]. Finally, the results should help the clinicians in the proper optimization of anticoagulant therapy through personalization of treatment approaches based on the balanced insight into the risks and advantages to elderly AF patients [8].

MATERIALS AND METHODS:

This comparative observational research carried out at the School of Pharmacy of the University of Management and Technology Lahore between June 2024 and May 2025. Evidence was to be provided on the safety and efficacy to compare and contrast two drugs, direct oral anticoagulants (DOACs) and warfarin, in old age adults with atrial fibrillation (AF). The sample used in the study was a population of 120 subjects who were elderly (aged 65 years or more), diagnosed and treated with oral anticoagulant therapy of non-valvular atrial fibrillation.

A purposive sampling technique was used to select the participants in affiliated healthcare facilities and outpatient clinics. Inclusion criteria comprised patients 65 years or older with a confirmed diagnosis of non-valvular atrial fibrillation, and, undergoing either a DOAC (dabigatran, rivaroxaban, apixaban, or edoxaban) or warfarin, continuing usage of which had been at least six months before enrollment. Patients who had valvular heart disease, patients with a mechanical heart valve, end-stage renal disease, severe hepatic dysfunction, patients with active malignancy, or those who were pregnant or lactating were excluded.

It was ensured that the patients in the cohort of the study were placed in 2 groups (Group A with n=60 and group B with n=60) depending on which anticoagulant therapy they received: DOACs or warfarin. Demographic data, clinical demographics, comorbidities history, present medications and laboratory results were collected on a structured data collection form. INR figures were noted by those using warfarin whilst renal function was assessed in those using DOAC.

The safety endpoint was based on major and minor episodes of bleeding which were categorized as per the limits of the International Society on Thrombosis and Haemostasis (ISTH). Major bleeding events were characterized into intracranial hemorrhage and gastrointestinal bleeding that requires transfusion or bleeding resulting in hospitalization or death. Any clinically discernible bleeding that failed to fulfill the requirements of major bleeding was considered as minor bleeding.

Primary outcome assessment was done by measuring the prevention of thromboembolic events, specifically ischaemic stroke and systemic embolism, during the study period. Patient records were looked upon at least monthly and follow-up interviews were carried out via clinic visits and telephone interview to make sure that there was no data shortcomings of the adverse event and therapeutic results.

The SPSS version 26 was used in data analysis. Age, weight, and treatment duration were continuous variables that were reported as the mean and standard devagation (SD) whereas gender, nature of bleeding, and presence or absence of thromboembolic events were categorical variables that were reported as frequencies and percentages. A chi-square test was chosen to compare categorical results between the two groups, whereas independent sample t-tests were performed in the case of continuous variables. A p-value less than 0.05 was regarded to be significant.

Ethical consideration was not left out. Before the act, a consent form was signed by every patient or their guardian. The protocol of the study was approved and reviewed by the Institutional Review Board (IRB) School of Pharmacy, University of Management and Technology, Lahore. The patient information privacy and confidentiality were highly observed during the study period.

This approach allowed to compare the DOACs and warfarin comprehensively regarding safety and efficacy because it provides useful information about the best use of anticoagulants in old patients with atrial fibrillation.

RESULTS:

This research was carried out at School of Pharmacy, University of Management and Technology, Lahore June 2024 to May 2025. One hundred and twenty elderly patients with Atrial Fibrillation (AF) were recruited and randomly divided into two equal groups where 60 patients underwent Direct Oral Anticoagulants (DOACs) therapy, and the 60 patient cases were applied to Warfarin therapy. The main measures of outcome were the occurrence of major bleeds, the development of stroke, and the maintenance of International Normalized Ratio (INR). The secondary outcomes were patient compliance, minor bleeding incidences, and overall mortality during study period.

Table 1: Comparison of Efficacy Outcomes between DOACs and Warfarin Groups:

Outcome	DOACs Group (n=60)	Warfarin Group (n=60)	p-value
Stroke occurrence	2 (3.3%)	7 (11.7%)	0.043*
Systemic embolism	1 (1.7%)	4 (6.7%)	0.178
INR within target range	N/A	28 (46.7%)	—
Mortality (all-cause)	1 (1.7%)	3 (5.0%)	0.309

Table 1 presents the overview of comparative efficacy of DOACs and Warfarin in thromboembolic preventative measures (Table 1). The prevalence of stroke was found to be statistically significant, with the DOACs group having the lower prevalence (3.3 %) as compared to that of the Warfarin group (11.7 %) and the p value of 0.043. Systemic embolism was experienced in 1 patient in DOACs patients (1.7 percent) contrasted with 4 patients (6.7 percent) in Warfarin drugs; however, the distinction was not clear ($p = 0.178$). The stable range with the INR was confined to the Warfarin group only where few patients (46.7%) had attained a stable therapeutic range and hence a notable weakness of the Warfarin treatment. There was low mortality in both the groups over the period of one year and the difference was not statistically significant ($p = 0.309$).

Table 2: Comparison of Safety and Tolerability between DOACs and Warfarin Groups:

Outcome	DOACs Group (n=60)	Warfarin Group (n=60)	p-value
Major bleeding events	1 (1.7%)	6 (10.0%)	0.049*
Minor bleeding events	4 (6.7%)	10 (16.7%)	0.093
Discontinuation due to AEs	1 (1.7%)	4 (6.7%)	0.178
Adherence (good compliance)	55 (91.7%)	41 (68.3%)	0.002*

The safety and tolerability levels of the two treatment regimens are contained in Table 2. The incidence of major bleeding was remarkably low in the DOACs group (1.7%) than the Warfarin group (10.0%) and the p-value was 0.049 showing the superior safety of DOACs. Episodes of minor bleeding occurred more often in the Warfarin group (16.7%) than the DOACs group (6.7%) though the outcome was not significant ($p = 0.093$). Warfarin (6.7 per cent) was less likely to be stopped in the treatment of AEs than DOACs (1.7 per cent), but the result did not reach a significant value ($p = 0.178$). Notably, the proportion of patient adherence was much higher among the DOAC users (91.7%), than the Warfarin users (68.3%), and the p-value was highly significant at 0.002.

The above results indicated that DOACs have proven to reduce the risk of stroke in addition to less bleeding effects and high patient compliance as opposed to Warfarin. Easier adherence in the DOAC group may be explained by a lower requirement and frequency of INR controls and fewer diet restrictions.

DISCUSSION:

The current work offered a full comparative analysis of direct oral anticoagulants (DOACs) and warfarin efficacies and safety in older adults with atrial fibrillation (AF). Aged patients represented the most vulnerable group as the change of physiology aggravated due to age, other numerous comorbidities, and polypharmacy, which affected the choice of anticoagulants and their effectiveness [9]. This study findings were compatible with the emerging clinical evidence advocating preference of DOAC over warfarin in the majority of elderly patients with non-valvular AF.

Regarding efficacy, DOACs have shown a similar or better capability of preventing thromboembolic events, such ischemic stroke and systemic embolism, than warfarin. The incident of stroke was statistically significantly lower in patients who received DOACs indicating that anticoagulation control was more successful [10]. It was to a large extent due to more predictable pharmacokinetics and pharmacodynamics of DOACs, there was no need to monitor INR routinely, and their effects on the body were less influenced by food intake or other medications compared to warfarin. Besides, the quick onset/offset of the DOACs permitted the enhanced management around surgical procedures or bleeding incidents, making them more useful in elderly patients [11].

Concerning safety, the rate of a serious bleeding incident, especially intracranial hemorrhage, was a lot lower in the DOAC subject group. This resounded the trials and real-world evidence of earlier trials on a large scale. Although effective a limited therapeutic range and increased risk of variable INR levels which partially resulted in either subtherapeutic or supratherapeutic anticlotting [12] were seen with warfarin. They were more frequent in old age, when older individuals would have problems with the preservation of medication, diet adherence and variability of renal functioning. On the contrary, the DOACs were considered to offer consistent anticoagulation profiles without the need to frequently test and measure blood and thus have a less burden on patients and healthcare providers.

It was however necessary to mention that not all DOACs acted the same and also renal functioning was extremely important in the choice and dose of dabigatran, rivaroxaban, apixaban and edoxaban [13]. Renal impairment that was higher in the elderly patients required special consideration as the dose adjustments had to be made so that safety is not compromised but efficacy is still not compromised. In spite of these factors, it was noted that the general safety profile of DOACs was very encouraging in different levels of renal functions provided that they were used in their appropriate doses.

Moreover, the level of adherence seemed to be higher in the DOAC group probably because of the lack of INR monitoring and a reduced amount of dietary restrictions. This aspect must have led to the better clinical outcomes realized. Moreover, the easy administration scheme of DOACs could have contributed to higher adherence rates as well as the decreased likelihood of complications arising due to incorrect application [14].

The study had one such limitation, as there was a possibility of selection bias where patients with more bleeding risk might have been earlier initiated on DOACs. Moreover, the authors failed to consider the socioeconomic side and the economic implication that may affect long-term adherence, particularly in low-resource environment. However, the summative evidence was in agreement with the conclusion about DOACs providing a superior risk-benefit profile compared to warfarin among the elderly patients with AF [15].

Summing up, during the comparative assessment, it became clear that DOACs presented an improved safety profile, fewer strokes, and improved adherence among elderly patients with atrial fibrillation. All these findings implied that the use of DOACs might be viewed as the optimal anticoagulation treatment in this patient group with references to covering individual patient-related characteristics, including their kidney health and the affordability of drugs.

CONCLUSION:

The present research found that Direct oral anticoagulants (DOACs) were superior to warfarin in atrial fibrillation among the elderly. Patients who received DOACs had much fewer events of major bleeding incidents that included intracerebral hemorrhages as compared to those who received warfarin. Besides, DOACs proved to have similar or better effectiveness in the prevention of such thromboembolic event like stroke and systemic embolism. The frequency of follow-ups, diet restrictions, and dosage changes, which is often associated with warfarin, were much lower in the DOAC patients and promoted patient compliance and overall quality of care. Besides, the decreased risk of adverse events and simplified dosing schedules delivered by DOACs made the latter a more attractive choice in older people with atrial fibrillation. In light of these results, DOACs had superior risk-benefit ratio, and offered a welcome alternative to warfarin among the older segment of the population. Nevertheless, the decision to use anticoagulant treatment was still based on individual patient characteristics and clinical judgment.

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