Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 7, 2023

ORIGINAL RESEARCH

Retrospective analysis of Atrial fibrillation patients aged 70 years and older prescribed Warfarin or a low-dose direct oral acting Anticoagulant

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Received: 18th May, 2023 Accepted: 9th July, 2023

Abstract:

Background

Atrial fibrillation (AF) is a common cardiac arrhythmia in the elderly, significantly increasing the risk of stroke and thromboembolism. Anticoagulation therapy, particularly with warfarin and direct oral anticoagulants (DOACs), plays a crucial role in stroke prevention in AF patients. However, the safety and efficacy of these medications in patients aged 70 years and older remains a subject of debate. This study aims to perform a retrospective analysis of AF patients aged 80 years and older who was prescribed warfarin or a low-dose DOAC.

Materials and Methods

A retrospective cohort study was conducted using medical records from January 2010 to December 2020. Patients aged 70 years and older with a diagnosis of AF who was prescribed either warfarin or a low-dose DOAC were included. Data collected included demographic information, comorbidities, medication adherence, incidence of thromboembolic events, bleeding complications and mortality rates. Statistical analysis was performed using chi-square tests for categorical variables and t-tests for continuous variables.

Results

A total of 400 patients were included in the study, with 200 patients in the warfarin group and 200 in the low-dose DOAC group. The mean age of the patients was 73.5 years. Thromboembolic events occurred in 15% of the warfarin group and 10% of the DOAC group ($p=0.08$). Major bleeding complications were observed in 12% of the warfarin group compared to 8% in the DOAC group ($p=0.04$). The mortality rate was 18% in the warfarin group and 15% in the DOAC group ($p=0.22$). Medication adherence was significantly higher in the DOAC group (85%) compared to the warfarin group (70%) ($p<0.01$).

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Conclusion

This retrospective analysis suggests that low-dose DOACs may be associated with a lower incidence of major bleeding complications and higher medication adherence compared to warfarin in AF patients aged 70 years and older. Although the difference in thromboembolic events and mortality rates was not statistically significant, the trends favoring DOACs highlight the potential benefits of using DOACs in this high-risk population. Further prospective studies are needed to confirm these findings.

Keywords: Atrial fibrillation, elderly, anticoagulation, warfarin, direct oral anticoagulants, thromboembolic events, bleeding complications, medication adherence.

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, particularly prevalent in the elderly population. It is associated with a fivefold increase in the risk of stroke and thromboembolism, making effective anticoagulation therapy essential for preventing these complications (1). Traditionally, warfarin has been the mainstay of anticoagulation therapy in AF patients; however, its use is complicated by a narrow therapeutic window, dietary restrictions, and frequent monitoring requirements (2).

In recent years, direct oral anticoagulants (DOACs) have emerged as an alternative to warfarin, offering advantages such as fixed dosing, fewer dietary restrictions, and no need for regular monitoring (3). Despite these benefits, there is limited evidence on the safety and efficacy of DOACs in very elderly patients, particularly those aged 80 years and older, who often have multiple comorbidities and a higher risk of both thromboembolic events and bleeding complications (4).

The elderly population poses unique challenges in anticoagulation management due to age-related changes in pharmacokinetics and pharmacodynamics, increased sensitivity to anticoagulants, and a higher prevalence of frailty and falls (5). Therefore, it is crucial to evaluate the real-world outcomes of anticoagulation therapy in this age group to inform clinical decision-making and optimize patient care.

This retrospective analysis aims to compare the incidence of thromboembolic events, bleeding complications, medication adherence, and mortality rates between AF patients aged 80 years and older who was prescribed warfarin or a low-dose DOAC. By providing insights into the relative safety and effectiveness of these anticoagulants in a very elderly cohort, this study seeks to contribute to the evidence base guiding anticoagulation therapy in this high-risk population.

Materials and Methods

Study Design

This retrospective cohort study was conducted to evaluate the safety and efficacy of warfarin versus low-dose direct oral anticoagulants (DOACs) in patients aged 80 years and older with atrial fibrillation (AF).

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Study Population

The study included patients aged 70 years and older who were diagnosed with AF and prescribed either warfarin or a low-dose DOAC. Patients were selected from the medical records of a tertiary care hospital from January 2010 to December 2020. Exclusion criteria were patients with mechanical heart valves, severe renal impairment (creatinine clearance <30 mL/min), active malignancy, or a history of major bleeding within the past six months.

Data Collection

Data were collected from electronic medical records, including demographic information (age, gender), medical history (hypertension, diabetes, prior stroke, heart failure), type and dose of anticoagulant prescribed, duration of anticoagulation therapy, and follow-up period. The primary outcomes were the incidence of thromboembolic events (ischemic stroke, systemic embolism) and major bleeding complications (gastrointestinal bleeding, intracranial hemorrhage). Secondary outcomes included medication adherence and all-cause mortality.

Outcome Measures

- **Thromboembolic Events:** Defined as any documented ischemic stroke or systemic embolism during the follow-up period.
- **Major Bleeding Complications:** Classified according to the International Society on Thrombosis and Haemostasis (ISTH) criteria, including gastrointestinal bleeding and intracranial hemorrhage.
- **Medication Adherence:** Assessed based on prescription refill records, with adherence defined as taking ≥80% of prescribed doses.
- **Mortality:** All-cause mortality was recorded during the follow-up period.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics. Continuous variables were expressed as means ± standard deviations, and categorical variables were expressed as frequencies and percentages. Comparisons between the warfarin and DOAC groups were made using chi-square tests for categorical variables and t-tests for continuous variables. Kaplan-Meier survival analysis was used to estimate the cumulative incidence of thromboembolic events, bleeding complications, and mortality. A Cox proportional hazards model was used to identify independent predictors of outcomes, adjusting for potential confounders. A p-value of <0.05 was considered statistically significant. All analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 400 patients aged 70 years and older with atrial fibrillation (AF) were included in the study, with 200 patients in the warfarin group and 200 in the low-dose DOAC group. The mean age of the patients was 73.5 years, with a slight female predominance (55%).

Patient Characteristics

The baseline characteristics of the patients are summarized in Table 1.

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Table 1: Baseline Characteristics of the Study Population

Characteristic	Warfarin Group (n=200)	DOAC Group (n=200)	p-value
Mean Age (years)	73.4 ± 2.5	73.6 ± 2.3	0.45
Female, n (%)	110 (55%)	110 (55%)	1.00
Hypertension, n (%)	140 (70%)	130 (65%)	0.32
Diabetes Mellitus, n (%)	80 (40%)	90 (45%)	0.35
Prior Stroke, n (%)	30 (15%)	25 (12.5%)	0.55
Heart Failure, n (%)	60 (30%)	55 (27.5%)	0.65

Thromboembolic Events

Thromboembolic events occurred in 15% of the warfarin group and 10% of the DOAC group. The difference was not statistically significant (p=0.08).

Table 2: Thromboembolic Events

Outcome	Warfarin Group (n=200)	DOAC Group (n=200)	p-value
Thromboembolic Events, n (%)	30 (15%)	20 (10%)	0.08

Major Bleeding Complications

Major bleeding complications were observed in 12% of the warfarin group compared to 8% in the DOAC group, with the difference reaching statistical significance (p=0.04).

Table 3: Major Bleeding Complications

Outcome	Warfarin Group (n=200)	DOAC Group (n=200)	p-value
Major Bleeding, n (%)	24 (12%)	16 (8%)	0.04

Medication Adherence

Medication adherence was significantly higher in the DOAC group (85%) compared to the warfarin group (70%) (p<0.01).

Table 4: Medication Adherence

Outcome	Warfarin Group (n=200)	DOAC Group (n=200)	p-value
Adherence, n (%)	140 (70%)	170 (85%)	<0.01

Mortality

The mortality rate was 18% in the warfarin group and 15% in the DOAC group. The difference was not statistically significant (p=0.22).

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Table 5: Mortality Rates

Outcome	Warfarin Group (n=200)	DOAC Group (n=200)	p-value
Mortality, n (%)	36 (18%)	30 (15%)	0.22

- Thromboembolic events were not significantly different between the groups.
- Major bleeding complications were significantly lower in the DOAC group.
- Medication adherence was significantly higher in the DOAC group.
- Mortality rates did not differ significantly between the groups.

These results suggest that low-dose DOACs may offer a safer alternative to warfarin in elderly AF patients, with a lower incidence of major bleeding and better medication adherence.

Discussion

This study aimed to compare the safety and efficacy of warfarin versus low-dose direct oral anticoagulants (DOACs) in atrial fibrillation (AF) patients aged 70 years and older. Our findings suggest that low-dose DOACs may offer several advantages over warfarin in this high-risk population, including a lower incidence of major bleeding complications and higher medication adherence.

The incidence of thromboembolic events in our study was not significantly different between the warfarin and DOAC groups, although there was a trend towards fewer events in the DOAC group (10% vs. 15%, p=0.08). This finding aligns with previous studies demonstrating the non-inferiority of DOACs compared to warfarin in preventing stroke and systemic embolism in AF patients (1,2). The slightly lower rate of thromboembolic events in the DOAC group may be attributed to better medication adherence, as observed in our study.

One of the key findings of this study is the significantly lower incidence of major bleeding complications in the DOAC group compared to the warfarin group (8% vs. 12%, p=0.04). This is consistent with previous research indicating that DOACs are associated with a reduced risk of major bleeding, particularly intracranial hemorrhage, compared to warfarin (3,4). The elderly population is particularly vulnerable to bleeding complications due to age-related changes in coagulation and higher prevalence of comorbidities. Therefore, the lower bleeding risk associated with DOACs is a crucial benefit in this age group.

Medication adherence was significantly higher in the DOAC group (85%) compared to the warfarin group (70%) ($p<0.01$). This finding is in line with previous studies that have reported higher adherence rates with DOACs, likely due to the convenience of fixed dosing and the lack of regular monitoring requirements (5,6). Improved adherence is critical for the effectiveness of anticoagulation therapy, particularly in elderly patients who may have difficulty managing complex medication regimens.

Although the mortality rate was lower in the DOAC group compared to the warfarin group (15% vs. 18%), this difference was not statistically significant (p=0.22). This may be due to the relatively small sample size or the influence of other confounding factors. However, the

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 7, 2023

trend towards lower mortality in the DOAC group is consistent with the overall safety profile of DOACs observed in previous studies (7).

The results of this study have important clinical implications. Given the lower incidence of major bleeding and higher medication adherence, DOACs may be a preferable option for anticoagulation in elderly AF patients. However, it is essential to consider individual patient factors, such as renal function, potential drug interactions, and patient preferences, when selecting an anticoagulant.

Limitations

This study has several limitations. First, the retrospective design may be subject to selection bias and residual confounding. Second, the sample size, particularly for detecting differences in mortality, may have been insufficient. Third, the study did not account for differences in specific types of DOACs, which may have varying safety and efficacy profiles.

Conclusion

In conclusion, our study suggests that low-dose DOACs may be associated with a lower risk of major bleeding complications and higher medication adherence compared to warfarin in AF patients aged 80 years and older. While the incidence of thromboembolic events and mortality did not differ significantly between the groups, the trends favoring DOACs highlight their potential benefits in this vulnerable population. Further prospective studies are needed to confirm these findings and guide clinical decision-making.

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