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RESEARCH ARTICLE
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EVALUATING THE RISK-BENEFIT PROFILE OF RIVAROXABAN VERSUS WARFARIN IN STROKE PREVENTION AMONG ELDERLY PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION; A RETROSPECTIVE COHORT STUDY

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Abstract

Background and Aim: Non-valvular atrial fibrillation (NVAF) is particularly common in the elderly, with more than 50% of NVAF patients over 80 years of age. The present study aimed to assess the risk-benefit profile of Rivaroxaban versus Warfarin in stroke prevention among patients with non-valvular atrial fibrillation.

Patients and Methods: This retrospective cohort study evaluated 100 NVAF patients treated with Warfarin or Rivaroxaban in the Department of Pharmacology in collaboration with Cardiology Unit of Tertiary Care Hospital, Lahore from April 2022 to April 2024. All the patients were categorized into two groups; Group-I (Rivaroxaban treated patients, N=50) and Group-II (Warfarin treated patients, N=50). The prescription of rivaroxaban, appropriate dosing, non-gastrointestinal bleeding (NGIB), ischemic stroke, and gastrointestinal bleeding (GIB) were different outcomes measured during investigation. Data analysis was done using SPSS version 27.

Results: The overall mean age was 66.4±11.4 years with an age range 16-80 years. Of the total 100 NVAF patients, there were 52% male and 48% female. Patient's distribution based on their age groups were as follows; 14 (14%) in 16-40 years, 32 (32%) in 41-60 years, and 54 (54%) in ≥60 years. Hypertension, diabetes, and congestive heart failure were the most prevalent comorbidities found in 74%, 56%, and 38%, respectively. Statins, proton pump inhibitors, and non-steroidal anti-inflammatory drugs (NSAIDs) like aspirin were the most prevalent prescribed medication given to 69% vs. 71%, 43% vs. 40%, and 29% vs. 17%, respectively. No significant variance was seen in terms of non-gastrointestinal bleeding (NGIB) and risk of ischemic stroke between both groups.

Conclusion: The present investigation observed that the rivaroxaban and warfarin groups showed no significant variance in the prevention of stroke among NVAF elderly patients. In addition, it demonstrated short- and long-term safety and efficacy in stroke prevention for NVAF patients, and both the agents could be used as anticoagulants.

Keywords: Ischemic stroke, Rivaroxaban, Warfarin, Non-valvular atrial fibrillation

INTRODUCTION

Atrial fibrillation (AF) is a prevalent heart condition that primarily affects older adults (≥70 years). Non-valvular atrial fibrillation (NVAF) is particularly common in the elderly, with more than 50% of NVAF patients over 80 years of age [1, 2]. Atrial fibrillation (AF) is the most common chronic cause of stroke, with high mortality and morbidity [3]. Patients with NVAF exhibit higher rates of hypertension, cardiovascular disease, and diabetes mellitus (DM) [3, 4]. An earlier study reported that non-valvular atrial fibrillation (NVAF) accounts for 84% of AF cases [5]. NVAF patients have a fivefold increased risk of thromboembolic ischemic stroke compared with non-NVAF patients.

Direct anticoagulants (DOACs) are recommended as the standard treatment for the prevention of thromboembolic events in patients with NVAF [6]. Newer DOACs, such as rivaroxaban, are approved and generally do not require routine follow-up with screening and blood tests, unlike warfarin. DOACs provide a more effective anticoagulant regimen when compared with warfarin. There may be one or more risk factors in patients with NVAF, such as hypertension, transient ischemic attack, advanced age, and heart disease [7-9]. The rivaroxaban utilization has been augmented by warfarin causing allergy and poor outcomes in stroke prophylaxis. Rivaroxaban 20 mg dose is routinely used for NVAF patients, whereas the dose is reduced to 15 mg in renal impairment cases [10]. Majority of Western study focused on the safety and efficacy of warfarin and rivaroxaban for treating NVAF cases. A limited literature was found in Pakistan regarding how the global variation in clinical characteristics of AF patients has created problems in selecting appropriate treatment. [11, 12].

METHODOLOGY

This retrospective cohort study evaluated 100 NVAF patients treated with Warfarin or Rivaroxaban in the Department of Pharmacology in collaboration of Cardiology Unit of Tertiary Care Hospital, Lahore from April 2022 to April 2024. All the patients were categorized into two groups; Group-I (Rivaroxaban treated patients, N=50) and Group-II (Warfarin treated patients, N=50). The study included adult patients aged 16 years and older with a new diagnosis of NVAF and treated with warfarin or rivaroxaban. Outcomes were defined as ischemic stroke, GIB, and NGIB leading to hospitalization, where rates of each outcome were recorded. The prescription of rivaroxaban, appropriate dosing, non-gastrointestinal bleeding (NGIB), ischemic stroke, and gastrointestinal bleeding (GIB) were different outcomes measured during investigation.

Data analysis was done using SPSS version 27. Frequencies and percentages were reported for categorical variables. Mean and standard deviation were used to plot continuous variables, and Student's t-test which are summarized. Differences between the warfarin and rivaroxaban groups were analyzed.

RESULTS

The overall mean age was 66.4±11.4 years with an age range 16-80 years. Of the total 100 NVAF patients, there were 52% male and 48% female. Hypertension, diabetes, and congestive heart failure were the most prevalent comorbidities found in 74%, 56%, and 38%, respectively. Statins, proton pump inhibitors, and non-steroidal anti-inflammatory drugs (NSAIDs) like aspirin were the most prevalent prescribed medication given to 69% vs. 71%, 43% vs. 40%, and 29% vs. 17% respectively. No significance variance was seen in terms of non-gastrointestinal bleeding (NGIB) and risk of ischemic stroke between both groups. Patient's distribution based on their age groups were as follows; 14 (14%) in 16-40 years, 32 (32%) in 41-60 years, and 54 (54%) in ≥60 years as shown in Figure-1. Figure-2 illustrate the different comorbidities of NVAF patients. Table-I presents the demographic data, baseline details, and Comorbidities compared in both groups. Different medications given to both groups are shown in Table-II. The appropriateness of rivaroxaban dosing and prescribing was assessed based on specific criteria is shown in Table-III. Outcomes of rivaroxaban and warfarin groups are compared in Table-IV.

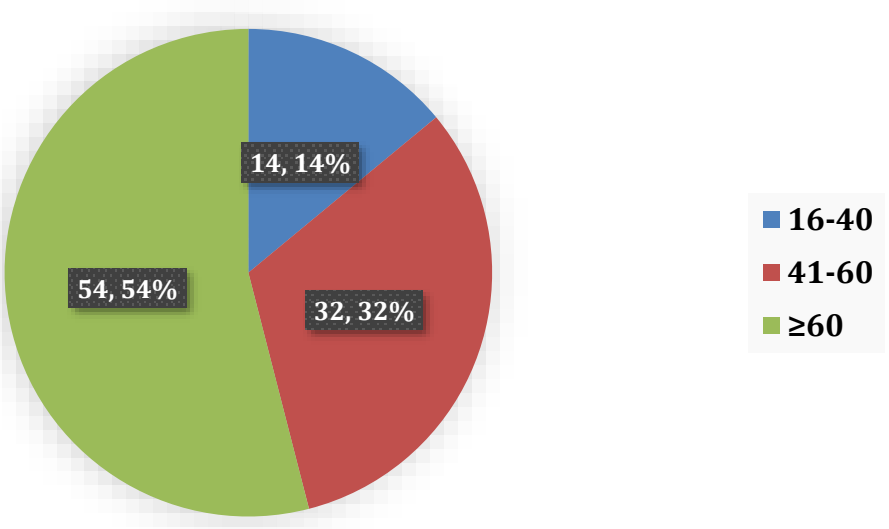

Figure-1 Age groups (N=100)

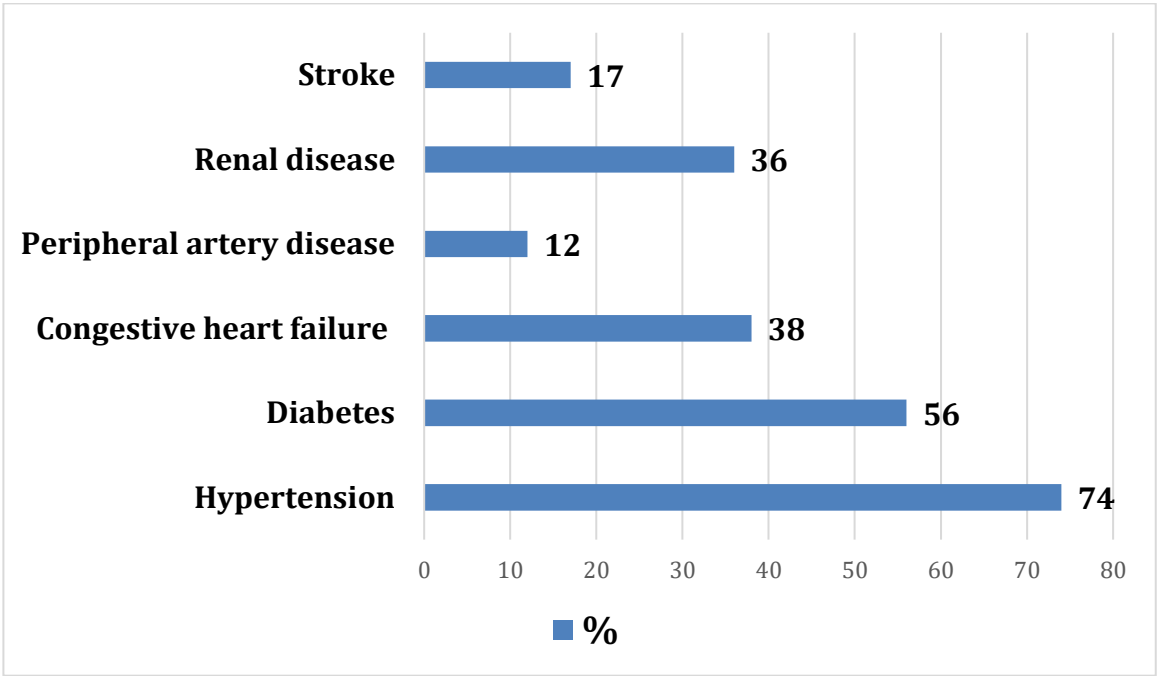

Figure-2 different comorbidities of NVAF patients (N=100)

Table-I demographic data, baseline details, and Comorbidities compared in both groups (N=100)

Variables	Group-I (N=50)	Group-II (N=50)	P-value
Age (years)	64.68±13.84	68.12±8.96	0.025
Age-groups (years)			0.025
16-40	6 (12%)	8 (16%)	
41-60	14 (28%)	18 (36%)	
≥60	22 (44%)	32 (64%)	
Gender N (%)			0.689
Male	22 (44%)	30 (60%)	
Female	28 (54%)	20 (40%)	
Comorbidities N (%)			<0.001
Hypertension	40 (80%)	34 (68%)	
Diabetes	30 (60%)	24 (48%)	
Congestive heart failure	20 (40%)	18 (36%)	
Peripheral artery disease	5 (10%)	7 (14%)	
Renal disease	22 (44%)	14 (28%)	
Stroke/ transient ischaemic attack	10 (20%)	7 (14%)	

Table-II Medications

Medications	Group-I (N=50)	Group-II (N=50)
Statins	69%	71%
Proton pump inhibitors	43%	40%
NSAIDs	29%	17%
Antidepressants	8%	8%
Antiplatelet	7%	7%

Table-III appropriateness of rivaroxaban dosing and prescribing

Dose	Group-I (N=50)
10 mg	0
15 mg	16
20 mg	34
Overall Appropriate	47

Table-IV Outcomes of rivaroxaban and warfarin groups

Outcomes	Group-I (N=50) N (%) IR*	Group-II (N=50) N (%) IR	HR (95% CI) P-value
Stroke	6 (12%) 0.5	11 (22%) 0.5	1.0 (0.3-3.2) 0.6
Gastrointestinal bleeding (GI)	33 (66%) 2.8	14 (28%) 1.7	5.4 (2.7-10.9) 0.001
Non-gastrointestinal Bleeding (NGIB)	11 (22%) 0.6	25 (50%) 0.6	0.8 (0.3-1.8) 0.7

*IR; incidence rate HR; Hazard ratio

DISCUSSION

The present study mainly focused on the assessment of risk-benefit profile of Rivaroxaban versus Warfarin among NVAF patients for stroke prevention and reported rivaroxaban and warfarin groups showed no significance variance in the prevention of stroke among elderly patients with NVAF. In addition, it demonstrates short- and long-term safety and effectiveness in stroke prevention for NVAF patients. Regarding safety, the warfarin group showed less fatal bleeding and intracranial hemorrhage severity against rivaroxaban. However, higher rate of gastrointestinal bleeding in warfarin treated patients was observed [13-15]. In contrast, a previous study found that rivaroxaban exhibits higher gastrointestinal bleeding (GIB) against direct oral agents (DOACs). Likewise, GIB cases had higher susceptibility to bleeding due to various factors [16]. Age and bleeding history were the main factors for GIB severity.

Hypertension and diabetes mellitus (DM) accounted for one hundred co-morbidities; the highest percentage of each in both groups. This finding is consistent with results that showed hypertension,

DM and coronary artery disease were the most common comorbidities in patients with NVAF [17]. The increasing risk of stroke is significantly associated with prolonged diabetes among NVAF patients [18].

A higher prevalence of GIB was reported in rivaroxaban users than warfarin users, particularly in NVAF patients with three or more comorbidities in prior research. Furthermore, the rivaroxaban group had more cases of congestive heart failure (CHF) than the warfarin group [19, 20]. Studies describing anemia in patients with CHF showed an increased risk of GIB in patients with CHF using oral anticoagulants [21].

Ensuring the appropriate dose and prescription of rivaroxaban displayed higher effectiveness whereas limited patients utilized 15 mg dose despite their normal renal function. One study reported an increased incidence, with 16% of patients taking rivaroxaban, experiencing cognitive experience failure initiating rivaroxaban as a treatment [22]. An earlier study reported that the incidence of inappropriate dose of rivaroxaban received was present in 42% patients [23]. Similarly, the present study observed that the incidence of inappropriate dosing was lower than reported in previous studies. Antiplatelet dysfunction may have clinical significance, especially if it is NVAF-induced leading to a higher risk of ischemic stroke [24]. Even though, the study reported a small percentage (5%) were receiving inappropriate dosing for rivaroxaban: systematic review highlighted the importance of considering patients' opinions and preferences when choosing oral anticoagulants for patients with NVAF [25].

CONCLUSION

The present investigation observed that rivaroxaban and warfarin groups shown no significant variance in the prevention of stroke among NVAF elderly patients. In addition, it demonstrates short- and long-term safety and effectiveness in stroke prevention for NVAF patients, and that both agents could be used as anticoagulants.

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