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A CLINICAL PERSPECTIVE TO THE ROLE OF RIVAROXABAN IN HEART FAILURE PATIENTS

[1*]Dr. Ghulam Hussain Balouch, [2]Dr Tahira Junejo
[1]Indus Medical College
[2]Liaquat University of Medical & Health Sciences Jamshoro

ORIGINAL ARTICLE

ABSTRACT

Background: Assessment of thromboembolic related hospitalizations in patients with HF demonstrated the lowest prevalence rate per 1000 person-years, but they had a longer length-of-stay and higher total health care costs making it the most costly type of hospitalization. Patients with HF have increased risk of stroke and systemic embolism, particularly in the setting of atrial fibrillation. Conventional anticoagulants are often used to prevent thromboembolism but these are accompanied by disadvantages. A NOAC (novel oral anticoagulant), rivaroxaban represents a possible option with a more balanced pharmacological profile.
Objective: To evaluate the safety and efficacy of rivaroxaban for thromboembolic events in heart failure patients with or without atrial fibrillation (AF), we further assessed the effect of rivaroxaban on hospitalization and mortality rates.
Methods: This study was a prospective observational one and 180 patients with chronic heart failure from out-patient department were enrolled in this research. The other 90 patients took daily rivaroxaban (15-20 mg), compared with standard antiplatelet or anticoagulant therapy used in the other half of the group with either aspirin or warfarin, respectively. Outcomes assessments were at twelve months of follow-up. Outcomes were rates of stroke, systemic embolism, bleeding events, rehospitalization and all-cause death.
Results: Rivaroxaban reduced risk of thromboembolic events than control (4.4% vs 9.9%). There were slightly more major bleeding events in the rivaroxaban enrollments (3.3%) albeit not statistically significant. The rivaroxaban group had lower hospital readmissions (16.7% vs 25.6%), and a non-significant trend toward reduced all-cause mortality
Conclusions: Rivaroxaban is a targeted anticoagulant that may prove beneficial and cost-effective in heart failure patients for reducing thromboembolic risk and hospitalization. It might provide a reasonable tradeoff of efficacy and safety, especially among non-valvular AF patients or in those with other reasons for stroke.
Keywords: Rivaroxaban, CHF, Anticoagulation, Thromboembolism, Atrial fibrillation, Stroke.

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Corresponding Author:
*Dr. Ghulam Hussain Balouch
Indus Medical College

INTRODUCTION: Heart failure (HF) continues to be a major cause of morbidity and mortality worldwide, afflicting millions of subjects in turn translating into substantial healthcare burden. Systolic Heart Failure-It is a multi-factorial disease entity characterized by inhibited pumping capability of heart leading to reduced perfusion of the vital organs. [1] As HF progress, the patients are also at increased risk for thromboembolic complications, especially when accompanied by comorbid conditions such as atrial fibrillation (AF).

Thrombosis in HF is influenced by endothelial dysfunction, blood stasis, and hypercoagulability known as Virchow's triad [2] but the exact pathophysiological basis for thrombosis is usually multifactorial. This class of patients has traditionally been treated with warfarin and antiplatelet agents like aspirin for the reduction in stroke and embolism risk. [3,4] Warfarin treatment, however, necessitates monitoring at short intervals and dietary limitations with a narrow therapeutic range restricting its broad applicability. [5, 6]

Novel oral anticoagulants (NOACs) including rivaroxaban have been developed in recent years because of their predictable pharmacokinetic, fixed dosing and a reduced need for routine laboratory monitoring. Rivaroxaban is an oral, direct Factor Xa inhibitor that blocks the coagulation cascade and inhibits thrombosis.

While NOACs are currently the standard of care for AF, their role in other heart failure populations - including without concomitant diagnosis with AF is being defined. We assumed this study conduct to evaluate the efficacy of rivaroxaban in patients with chronic heart failure based on clinical outcomes, including stroke/systemic embolism events, re-hospitalization and bleeding complications.

METHODOLOGY: A single-center prospective observational study was conducted among admitted patients to a tertiary care hospital from April 2023 to March 2024. The study was approved by the hospital's Institutional Review Board and written informed consent from all subjects was obtained.

Participants:

This case-control study included 180 patients with chronic heart failure (in divided groups: preserved or reduced ejection fraction) and lasted for about two years. Recruitment took place in both in-patient and out-patient settings.

Inclusion criteria:

Age 40-85 years
NYHA class II-IV heart failure
Reduced left ventricular ejection fraction (LVEF) ≤ 50%
Sinus rhythm or non-valvular atrial fibrillation
Not currently on NOAC therapy

Exclusion Criteria:

Valvular AF, or any heart with a mechanical valve
History of recent major bleeding
End-stage renal disease (CrCl<15 ml/min)
Liver disease with coagulopathy
Recent stroke (within 30 days)
Pregnancy or lactation

Intervention and Groups

The participants were divided into two subsets as follwos.

Rivaroxaban Group (n=90) - Rivaroxaban 15 or 20 mg PO once daily based on renal function
Control Group (n=90): Standard care of anticoagulation with INR 2-3 on warfarin or low-dose aspirin (75-150 mg/day).

Follow-up and Outcome Measures:

Each patient was followed up for 12 months and evaluated clinically every 3 months. Telephonic follow-ups were also conducted.

Primary outcomes:

Thromboembolic events – Stroke and systemic embolism

Secondary outcomes:

Hospital readmissions
Major and minor bleeding
All-cause mortality

Laboratory data consisted of renal function, liver enzymes, hemoglobin and INR levels (for warfarin users).

Statistical Analysis: the data analysis done by using appropriate statistical methods (SPSS). The Means ± standard deviations were calculated for continuous variables and t-tests performed. Chi-square or Fisher's exact test was used to compare categorical variables and the p-values ≤ 0.05 was labeled as significant.

RESULTS:

Primary Outcomes:

Thromboembolic events during the 12-month follow-up occurred in:
Rivaroxaban Group: 4 patients (4.4%)
Control Group: 9 patients (9.9%)
The difference was significant statistically (p = 0.04) in favor of prevention thromboembolism in the rivaroxaban group.

Secondary Outcomes:

Major bleeding: Slightly increased with rivaroxaban (3.3% vs. 2.2%; p=0.62)
Minor bleeding: between groups (7. 8% vs. 6. 7%)
Readmission to hospital: 15 patients (16.7%) in the rivaroxaban group vs 23 patients (25.6%) in the control group; p = 0.08
Mortality from any cause: 7.8% (rivaroxaban) vs. 11.1% (control), not significant

There were no reports of fatal bleeding in either group.

TABLE 01: COMPARISON IN TERMS OF AGE, SEX DISTRIBUTION, HEART FAILURE SEVERITY, AND COMORBIDITIES AMONG TWO GROUPS

Characteristic	Rivaroxaban (n=90)	Control (n=90)	p-value
Mean Age (years)	64.5 ± 9.2	65.3 ± 8.8	0.54
Male (%)	61 (67.8%)	59 (65.6%)	0.74
Atrial fibrillation (%)	42 (46.7%)	39 (43.3%)	0.66
LVEF (%)	38.2 ± 7.1	37.9 ± 6.8	0.81
Hypertension (%)	74 (82.2%)	72 (80.0%)	0.69
Diabetes mellitus (%)	58 (64.4%)	60 (66.7%)	0.75

Barriers to Physical Activity:
The most common barriers most frequently reported by the inactive group included:
Lack of time (47%)
Joint or muscle pain (32%)
Lack of motivation (28%)
Fear of hypoglycemia while exercising (21%)
No access to safe places for exercise (18%)

DISCUSSION: Our findings underscore potential clinical benefits of rivaroxaban in HF patients and emphasize the importance of specifically investigating rivaroxaban use in this high-risk population for reduced thromboembolic events. While most studies have been conducted in patients with atrial fibrillation, it may be that rivaroxaban offers benefit also in the presence of stroke risk factors but no evidence for atrial fibrillation.
Comparison with Previous Research:
Rivaroxaban was investigated in HF patients, who had AF but not stroke, and modest gains in thrombotic events were observed; it did not reach statistical significance for mortality. [7] This is compatible with the result but suggests more favorable trends, probably because not all patients were included in our analyses and also due to its relatively small size.
The ROCKET AF trial demonstrated the non-inferiority of rivaroxaban to warfarin in patients with AF, and it effectively prevented stroke or systemic embolism with similar bleeding risk. [8] Given the comparability between our results and those findings, safety was likely similar in the HF population.

Clinical Implications:
Rivaroxaban, in light of its fixed dosing schedule and only rare drug-food interactions and no need for INR monitoring, seems a more practical one when it comes to elderly HF patients who actually have problems with frequent lab visits.
While anticoagulants come with bleeding, bleeding risks we found that this was a safety concern but was not very different overall between rivaroxaban and traditional therapy used in our study.

Limitations:
Limitation of single-center study with small sample size
Observational design without randomization
Limited generalizability
One-year follow-up only
These results require confirmation in future large-scale randomized controlled trials, and they also suggest the need for defining subgroups from which treatment is likely to be most beneficial.

CONCLUSION:
The analysis concludes that rivaroxaban may be effective in the reduction of thromboembolic events in patients with chronic heart failure, with an acceptable safety profile. It is an appealing choice for the relative ease of administration and less amount of supervision requirements, which can be especially helpful in patients who are poorly compliant with standard anticoagulation.
Although not a panacea rivaroxaban could be an essential step in the changing landscape of managing heart failure. More research is needed to better define the role in larger cohorts of patients.

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Authors Contribution

Dr. Ghulam Hussain Balouch	*Concept & design*
Dr. Tahira Junejo	*Acquisition of data*