



# Cost Consequence Analysis of Rivaroxaban versus Warfarin among Atrial Fibrillation Patients: A Single-Center Retrospective Chart Review

Bushra AlOtaibi<sup>1</sup>, Reem AlOtaibi<sup>1</sup>, Yazed AlRuthia<sup>2,3</sup>, and Ghadah Assiri<sup>2</sup>

<sup>1</sup>College of Pharmacy, King Saud University

<sup>2</sup>Department of Clinical Pharmacy, College of Pharmacy, King Saud University

<sup>3</sup>Pharmacoeconomics Research Unit, College of Pharmacy, King Saud University

## INTRODUCTION

- Atrial fibrillation (AF) is the most common type of treated heart arrhythmia.
- The prevalence of AF has significantly increased by 33% over the last 20 years.
- The prevalence of AF among patients with heart failure and stroke were estimated to be 15% and 14%, respectively, according to a single-center observational study in Saudi Arabia.
- AF is a major cause of stroke, heart failure, sudden death, and cardiovascular morbidity.
- The use of anticoagulants is believed to reduce the risk of serious complications of AF, such as stroke and myocardial infarction (MI).
- Several oral anticoagulants have approved for prophylaxis of stroke and MI among patients with AF, such as warfarin and rivaroxaban.
- Novel oral anticoagulant (NOAC), such as rivaroxaban, are more convenient for patients than warfarin since they do not require frequent monitoring and dose adjustment.
- The clinical and economic value of NOAC, such as rivaroxaban, in the management of AF patients has not been examined in Saudi Arabia using real-world data.

## OBJECTIVE(S)

- The aims of this study were to compare warfarin and rivaroxaban among AF patients with regard to:
  - The rates of a predefined composite outcome, which consisted of any event of ER visit, hospitalization, stroke, MI, and/or death within a 12-month follow-up period.
  - The annual direct medical costs (e.g., lab and imaging studies, ER visits, admissions, etc..).

## METHODS

- Study design**
  - A single-center retrospective cohort study.
  - Data were retrieved from electronic health records (EHRs).
- Study setting**
  - King Khalid University Hospital (KKUH) which is university-affiliated tertiary care center with more than 1600 beds and a cardiac center.
- Study duration**
  - Patients were **retrospectively** followed up for **12 months** and data from June 2020 to September 2021 were retrieved.
- Sample size**
  - The minimum sample size for this study was estimated to be 196 patients based  $\alpha=0.05$ ,  $\beta=0.2$ , power of 80%, and hazard ratio of 1.35 for warfarin.
- Inclusion criteria**
  - Patients aged  $\geq 18$  years.
  - Patients with AF without mitral valve stenosis.
  - Complete (non-missing) observations in EHRs.
- Exclusion criteria**
  - Patients on other anticoagulants (e.g., dabigatran).
  - Patients who were on rivaroxaban or warfarin less than 12 months.
  - Cancer patients.
  - Patients with Mitral valve stenosis.
- Study Variables**
  - Composite outcome : Stroke, MI, hospitalization, ER visits, and/or death.
  - Anthropometric variables: weight, height, BMI, etc...
  - Ae and gender.
  - Comorbidities (DM, HTN, DLP, etc..)
  - Labs and imaging studies (INR, CBC, LFTs, MRI, X-ray, etc)
  - Prescriptions medications and total daily dosages.
  - Costs of prescription medications and all utilized healthcare services.
- Statistical analysis**
  - Descriptive statistics** to describe the patient characteristics and costs for AF patients on warfarin and rivaroxaban.
  - Multiple logistic regression to compare the odds of the composite outcome between rivaroxaban and warfarin was conducted.
  - Propensity score matching and inverse probability weighting** to generate the **95% confidence limits** for both the effectiveness (e.g., composite outcome rates) and costs.
  - All statistical analyses conducted using SAS<sup>®</sup> version 9.4 (SAS institute, Cary, NC, United States).

## RESULTS

**Table 1.** Patients' baseline characteristics.

| Characteristic               | Oral Anticoagulant |                   | P-value | Total      |
|------------------------------|--------------------|-------------------|---------|------------|
|                              | Rivaroxaban        | Warfarin          |         |            |
| Gender, N(%)                 |                    |                   |         |            |
| Female                       | 91(64.08)          | 56(66.67)         | 0.694   | 147        |
| Male                         | 51(35.92)          | 28(33.33)         |         | 79         |
| Age, mean $\pm$ SD           | 72.14 $\pm$ 11.18  | 66.77 $\pm$ 13.47 | 0.0014  | 70.15      |
| Comorbidities, N (%)         |                    |                   |         |            |
| Diabetes                     | 84(59.15)          | 35(41.67)         | 0.0092  | 119(52.65) |
| Hypertension                 | 121(85.21)         | 49(58.33)         | <0.0001 | 170(75.20) |
| Heart failure                | 26(18.30)          | 13(15.48)         | 0.570   | 39(17.25)  |
| Cardiovascular disease (CVD) | 39(27.46)          | 11(13.10)         | 0.0110  | 50(22.12)  |
| Dyslipidemia                 | 74(52.11)          | 22(26.19)         | 0.0001  | 96(42.47)  |

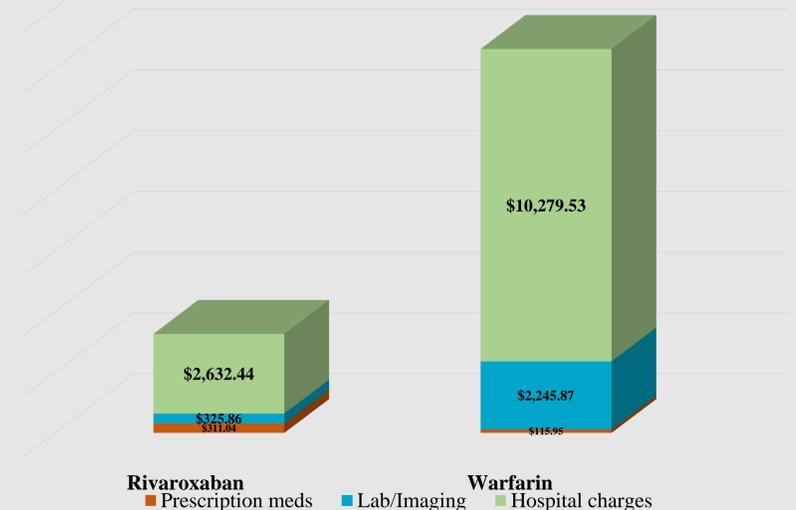
**Table 2.** Multiple logistic regression for the association between rivaroxaban (n=142) and warfarin (n=84) with the composite outcome (e.g., death or hospitalization).

| Variable                 | Odds ratio (OR) | P-value | 95% confidence interval |
|--------------------------|-----------------|---------|-------------------------|
| Rivaroxaban vs. Warfarin | 0.785           | 0.4430  | 0.427–1.446             |
| Age                      | 1.005           | 0.7087  | 0.981–1.029             |
| Female vs. male          | 1.539           | 0.1559  | 0.848–2.791             |
| Duration of illness      | 0.428           | 0.0189  | 0.210–0.869             |
| Heart failure            | 2.279           | 0.0336  | 1.066–4.873             |
| Cardiovascular disease   | 1.200           | 0.6091  | 0.596–2.415             |
| Diabetes mellitus        | 1.322           | 0.3703  | 0.718–2.437             |
| Hypertension             | 1.543           | 0.2573  | 0.729–3.268             |
| Dyslipidemia             | 1.006           | 0.9844  | 0.544–1.862             |

**Table 3.** The cost consequence analysis of rivaroxaban versus warfarin for the management of atrial fibrillation (AF).

|  | Rivaroxaban               | Warfarin                   | Mean difference (95% confidence interval) |
|--|---------------------------|----------------------------|---|
| Cost of treatment (USD), mean $\pm$ SD | 12,484.07 $\pm$ 34,354.55 | 62,212.06 $\pm$ 304,227.87 | -49,724.99 (-123563.26–-15076.03)         |
| Effectiveness rate, mean $\pm$ SD      | 0.54930 $\pm$ 0.4993253   | 0.54762 $\pm$ 0.5007166    | 0.00168 (-0.052101–0.18361)               |

**Figure 1.** Mean Annual Cost for Rivaroxaban & Warfarin



## CONCLUSIONS

- Rivaroxaban was associated with lower direct medical costs and had non-inferior effectiveness in preventing hospitalization and mortality among AF patients in comparison to warfarin.
- Future studies should examine the cost effectiveness of different NOACs against warfarin using larger samples and more robust study designs.

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