Rev Port Cardiol. 2014;33(9):535–544

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

ORIGINAL ARTICLE

Cost-effectiveness of rivaroxaban for stroke prevention in atrial fibrillation in the Portuguese setting

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Received 19 February 2014; accepted 23 February 2014
Available online 16 September 2014

KEYWORDS
Atrial fibrillation;
Cost-effectiveness;
Portugal;
Rivaroxaban;
Stroke

Abstract
Introduction and Aims: To project the long-term cost-effectiveness of treating non-valvular atrial fibrillation (AF) patients for stroke prevention with rivaroxaban compared to warfarin in Portugal.
Methods: A Markov model was used that included health and treatment states describing the management and consequences of AF and its treatment. The model's time horizon was set at a patient's lifetime and each cycle at three months. The analysis was conducted from a societal perspective and a 5% discount rate was applied to both costs and outcomes. Treatment effect data were obtained from the pivotal phase III ROCKET AF trial. The model was also populated with utility values obtained from the literature and with cost data derived from official Portuguese sources. The outcomes of the model included life-years, quality-adjusted life-years (QALYs), incremental costs, and associated incremental cost-effectiveness ratios (ICERs). Extensive sensitivity analyses were undertaken to further assess the findings of the model. As there is evidence indicating underuse and underprescription of warfarin in Portugal, an additional analysis was performed using a mixed comparator composed of no treatment, aspirin, and warfarin, which better reflects real-world prescribing in Portugal.
Results: This cost-effectiveness analysis produced an ICER of €3895/QALY for the base-case analysis (vs. warfarin) and of €6697/QALY for the real-world prescribing analysis (vs. mixed comparator). The findings were robust when tested in sensitivity analyses.

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http://dx.doi.org/10.1016/j.repc.2014.02.020

Conclusion: The results showed that rivaroxaban may be a cost-effective alternative compared with warfarin or real-world prescribing in Portugal.

PALAVRAS-CHAVE
Fibrilhação Auricular;
Custo-efetividade;
Portugal;
Rivaroxabano;
AVC

Estudo de custo-efectividade de rivaroxabano para prevenção de acidente vascular cerebral em doentes com fibrilhação auricular em Portugal

Resumo
Introdução e objetivos: Estimar o rácio custo-efetividade a longo-prazo associados à utilização de rivaroxabano na prevenção de acidente vascular cerebral em doentes com fibrilhação auricular (FA) não-valvular relativamente a varfarina em Portugal.
Métodos: Foi utilizado um modelo de Markov que representa os estádios representativos da progressão da FA e do seu tratamento. O horizonte temporal modelizado descreve o tempo de vida dos doentes e cada ciclo tem a duração de três meses. A análise foi desenvolvida na perspetiva da sociedade, tendo sido aplicada uma taxa de atualização de cinco por cento para custos e consequências. Os efeitos do tratamento foram obtidos no ensaio clínico de fase III ROCKET AF. Adicionalmente, no modelo foram incluídos valores de utilidade provenientes da literatura e estimativas de custos nacionais. Os *outcomes* avaliados no modelo incluem anos de vida incrementais, anos de vida ajustados pela qualidade de vida incrementais (AVAQ), custos incrementais e rácio custo-efetividade incremental (RCEI). Foram desenvolvidas análises de sensibilidade com o objetivo de avaliar os resultados do modelo. A evidência existente indica subutilização e subprescrição de varfarina em Portugal e, por esta razão, foi desenvolvida uma análise adicional com um comparador misto, constituído por não tratamento, ácido acetilsalicílico e varfarina, o que reflete melhor o «mundo real de prescrição».
Resultados: RCEI obtido varia entre 3 895€/AVAQ para o cenário-base (relativamente varfarina) e 6 697€/AVAQ para o «mundo real de prescrição» (relativamente comparador misto). As análises de sensibilidade demonstraram que os resultados são robustos.
Conclusão: Os resultados sugerem que rivaroxabano pode constituir uma alternativa custo-efetiva comparativamente a varfarina ou «mundo real de prescrição» em Portugal.

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disorder and constitutes an important risk factor for stroke,[1,2] associated with a five-fold risk[3]: 15% of all strokes are attributable to AF and around 25% of patients with ischemic stroke present AF.[4,5]

The prevalence of AF in the general population in developed countries is approximately 1.5–2%. In addition, the mean age of patients with this condition is steadily rising, such that it now averages between 75 and 85 years.[3] According to the FAMA (Atrial Fibrillation in Portugal) study, the prevalence of AF in the Portuguese population aged 40 and over is 2.5% (95% confidence interval [CI]: 2.2–2.8%) and increases with age, reaching 6.6% for individuals aged 70–79, and 10.4% for those aged 80 or more.[6]

Guidelines for stroke prevention in AF have been developed to encourage best practice and a systematic approach to treatment by physicians, with the intention of achieving the best outcome for the AF patient. The clinical guidelines on antithrombotic therapy for AF issued by the Portuguese National Coordinating Body for Cardiovascular Disease,[7] the European Society of Cardiology (ESC)[3] and the American Heart Association/American Stroke Association (AHA/ASA)[8] are generally accepted by the Portuguese medical community. Overall, these guidelines consider oral anticoagulants (OACs) the cornerstone of thromboembolic prevention in AF. Vitamin K antagonists (VKAs), primarily warfarin, are widely regarded as the current standard of care.

A meta-analysis of trials on antithrombotic therapy in the prevention of stroke in non-valvular AF shows that VKAs significantly reduce the risk of stroke by 64% vs. placebo.[9] Although effective, VKAs have limitations that make patient management challenging in practice.[10] For instance, the anticoagulation response to VKA treatment is unpredictable and is affected by genetic and environmental factors such as drug-drug and food-drug interactions. The high inter- and intra-patient variability in response to therapy means that frequent blood tests for international normalized ratio (INR) monitoring (an INR 2.0–3.0 is recommended) and dose adjustments are necessary.[11] The 2012 ESC guidelines state that new OACs such as rivaroxaban are generally preferable to VKAs in patients with non-valvular AF, when used as studied in the clinical trials performed to date.[3]

Over the past decade, risk factor scoring systems have been widely used to stratify the risk of thromboembolism