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ORIGINAL ARTICLE

Economic evaluation of dabigatran for stroke prevention in patients with non-valvular atrial fibrillation☆

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Abstract
Introduction and Objectives: To estimate the cost-effectiveness and cost-utility of dabigatran in the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation in Portugal.
Methodology: A Markov model was used to simulate patients' clinical course, estimating the occurrence of ischemic and hemorrhagic stroke, transient ischemic attack, systemic embolism, myocardial infarction, and intra- and extracranial hemorrhage. The clinical parameters are based on the results of the RE-LY trial, which compared dabigatran with warfarin, and on a meta-analysis that estimated the risk of each event in patients treated with aspirin or with no antithrombotic therapy.
Results: Dabigatran provides an increase of 0.331 life years and 0.354 quality-adjusted life years for each patient. From a societal perspective, these clinical gains entail an additional expenditure of 2978 euros. Thus, the incremental cost is 9006 euros per life year gained and 8409 euros per quality-adjusted life year.
Conclusions: The results show that dabigatran reduces the number of events, especially the most severe such as ischemic and hemorrhagic stroke, as well as their long-term sequelae. The expense of dabigatran is partially offset by lower event-related costs and by the fact that INR monitoring is unnecessary. It can thus be concluded that the use of dabigatran in clinical practice in Portugal is cost-effective.

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PALAVRAS-CHAVE
Acidente vascular cerebral;
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Portugal

Avaliação económica do dabigatrano na prevenção de acidentes vasculares cerebrais isquémicos em doentes com fibrilhação auricular não valvular

Resumo
Introdução e objetivos: Estimar os rácios custo-efetividade e custo-utilidade associados à utilização de dabigatrano na prevenção de acidentes vasculares cerebrais e embolias sistémicas em doentes com fibrilhação auricular não valvular em Portugal.
Metodologia: Foi utilizado um modelo de Markov para simular a evolução dos doentes, estimando a ocorrência de acidentes vasculares cerebrais isquémicos e hemorrágicos, de acidentes isquémicos transitórios, de embolias sistémicas, de enfartes agudos do miocárdio e de hemorragias intra e extracranianas. Os parâmetros clínicos baseiam-se nos resultados do estudo RE-LY, que compara a utilização de dabigatrano com a de varfarina, e numa meta-análise em que se estimou o risco de ocorrência de cada evento em doentes medicados com ácido acetilsalicílico ou sem qualquer terapêutica antitrombótica.
Resultados: O dabigatrano proporciona, a cada doente, um incremento de 0,331 e de 0,354 anos de vida ajustados pela qualidade. Na perspetiva da sociedade, estes ganhos clínicos implicam um aumento da despesa em 2.978 €. Assim, o custo incremental por ano de vida ganho é de 9.006 €, sendo o custo incremental por ano de vida ajustado pela qualidade de 8.409 €.
Conclusões: Os resultados obtidos mostram que o dabigatrano diminui a quantidade de eventos, nomeadamente os de maior gravidade como os acidentes vasculares cerebrais isquémicos e hemorrágicos, bem como as respetivas sequelas de longo prazo. Os custos com dabigatrano são parcialmente compensados por uma diminuição dos custos decorrentes dos eventos, bem como pela ausência de monitorização do INR. Assim, pode concluir-se que a utilização de dabigatrano na prática clínica portuguesa é custo-efetiva.

List of abbreviations

AF	atrial fibrillation
ICER	incremental cost-effectiveness ratio
INR	international normalized ratio
MI	myocardial infarction
QALY	quality-adjusted life years
TIA	transient ischemic attack
VAT	value-added tax

Introduction

Atrial fibrillation (AF) is a supraventricular arrhythmia characterized by deterioration of atrial mechanical function resulting in increased risk of thromboembolic events such as ischemic stroke.[1]

Non-valvular AF (i.e. not resulting from rheumatic mitral valve disease, prosthetic valves or valve repair[2]) is the most common sustained arrhythmia, increasing with age; it has an estimated prevalence of 1–2%, and this figure is set to rise with aging populations.[1] The overall prevalence of AF in the FAMA study, on a Portuguese population aged over 40, was 2.5%, but was significantly higher in those aged 70 or more (0.2% in those aged 40–49, 1.0% in those aged 50–59, 1.6% in those aged 60–69, 6.6% in those aged 70–79, and 10.4% in those aged 80 or over).[3] There were an estimated 143 000 cases in Portugal in 2012.

AF can be asymptomatic and remain undiagnosed: according to the Euro Heart Survey, only 69% of patients report symptoms.[4] Appropriate screening (pulse taking and electrocardiography) is not always performed in clinical practice; the estimated rate of detection of AF in primary health care is 64%.[5] There are also significant problems of patient awareness, as shown in the Portuguese FAMA study, in which only 62% of those with AF were aware of having the condition.[3]

The increased thromboembolic risk of these patients results in not only a doubling of mortality[1] but also increased morbidity, a consequence of the main complication of AF, ischemic stroke, the incidence of which is three to four times higher in AF,[6] which is thus one of the principal causes of ischemic stroke.[7] In the Framingham study, the annual risk of stroke attributable to AF was 1.5% for those aged 50–59 and 23.5% for those aged 80–89.[7] Furthermore, stroke associated with AF is generally more severe and leads to greater health care costs.[8]

The main treatment is currently vitamin K antagonists, usually warfarin, which reduces stroke risk by 64% compared to placebo and by 40% compared to aspirin.[9] However, the complications associated with its use, including interactions with other drugs and dietary considerations, as well as the difficulty in maintaining the international normalized ratio (INR) within therapeutic and safety limits, mean that many eligible patients are not medicated with warfarin. In Portugal, only 38% of those eligible for anticoagulation receive warfarin and 40% receive no antithrombotic therapy at all.[3]

These difficulties have prompted a search for alternative therapies that are at least as effective and safe as