VALUE IN HEALTH REGIONAL ISSUES 8C (2015) 36–42

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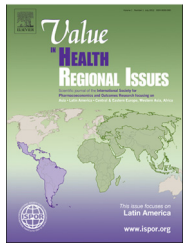

Cost-Effectiveness and Cost-Utility Analyses of Dabigatran Compared with Warfarin in Patients with Nonvalvular Atrial Fibrillation and Risk Factors for Stroke and Systemic Embolism within Brazilian Private and Public Health Care Systems Perspectives

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ABSTRACT

Objective: To analyze the cost-effectiveness and cost-utility of dabigatran compared with warfarin in patients with nonvalvular atrial fibrillation with moderate to high risk of ischemic stroke or systemic embolism and eligible for treatment with anticoagulants. **Methods:** Markov-based economic analysis was performed to estimate treatment costs and outcomes. Epidemiological and efficacy data were determined after a critical revision of the medical literature. Unit costs were taken from Brazilian official databases. Only direct medical costs were covered. Costs and benefits were discounted at a rate of 5% per year. Outcomes were expressed as life-year (LY) and quality-adjusted life-year (QALY). **Results:** Dabigatran use is cost-effective in terms of LY and QALY considering a willingness-to-pay threshold of 3 times gross domestic product per capita of 2010 (Brazilian real 57,048/US $24,275.74) per LY and QALY saved in both analyzed perspectives (private and public health care systems). **Conclusions:** Dabigatran use improves patient survival and quality of life compared with warfarin. This represents the best therapeutic option in terms of cost and effectiveness in the prevention of ischemic stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

Keywords: stroke prevention, atrial fibrillation, cost-effectiveness, cost-utility, dabigatran.

Introduction

Atrial fibrillation (AF) is a supraventricular arrhythmia in which an atrial electrical activity disorder occurs, causing the atria to lose their ability to contract, not generating atrial systole [1]. In population studies, AF is an important risk factor for ischemic stroke (IS), heart failure, and death [2], with a 3% to 6% annual risk of thromboembolic complications, which is 5 to 7 times greater than the risk in controls with a sinus rhythm [3].

The prevalence of AF is influenced by age, sex, presence of cardiovascular disease, such as valvular disease, and risk factors such as hypertension, diabetes, obesity, and insulin resistance [1,4]. Brazilian data show an annual incidence below 0.1% in the population younger than 40 years and 1.5% and 2.0% in men and women, respectively, older than 80 years [1].

More than 20% of all ISs are attributable to AF [4], thus representing the largest single cause and one of the most important risk factors for the occurrence of this condition in Brazil. The incidence of IS in patients with nonvalvular atrial fibrillation (NVAF) averages 5% per year [5].

AF is related to greater stroke severity, higher mortality, worse functional prognosis after stroke, greater recurrence, and longer hospital stays, resulting in larger and more significant costs to health care systems [6].

To reduce all these risks associated with AF, it is essential to rationally institute an anticoagulant therapy. Currently, therapy with vitamin K antagonists, especially warfarin, is the medication of choice for primary and secondary stroke prevention, transient ischemic attack, and other thromboembolic events in patients with AF at high risk for these events. This therapy, however, has

Conflict of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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2212-1099$36.00 – see front matter

http://dx.doi.org/10.1016/j.vhri.2015.02.003

a risk of bleeding events [7]. Therefore, there is an imminent need to establish new anticoagulant agents that are effective, safe, and more convenient to use.

Dabigatran etexilate is a small molecule that is rapidly absorbed after oral administration and converted into dabigatran acting directly by inhibiting thrombin, responsible for the conversion of fibrinogen into fibrin during coagulation cascade and preventing the development of thrombus (clot). In addition, dabigatran has proven its efficacy and safety without the need of coagulation monitoring and dose adjustments, and does not cause dietary restrictions for patients [8].

The objective of the present study was to determine the cost-effectiveness and cost-utility of the use of the new oral anticoagulant dabigatran compared with warfarin in patients with NVAF at risk for IS or systemic embolism and eligible for anticoagulant therapy.

Methods

Target Population

The modeled patient population comprised adults with NVAF at risk for IS or systemic embolism, eligible for treatment with an anticoagulant on the basis of CHADS and CHADSVASc scores. The CHADS2 score is a measure of the risk of stroke in which congestive heart failure, hypertension, an age of 75 years, and diabetes mellitus are each assigned 1 point and previous stroke or transient ischemic attack is assigned 2 points; the score is calculated by summing all the points for a given patient. The mean CHADS2 score in the model was 2.1. Of patients who entered the model, 63.6% were men aged 71 years, considering the predominant prevalence of AF in this age group, according to population-based studies [9].

Study Perspective

This study was developed from the perspectives of the Brazilian private health care system (Sistema de Saúde Suplementar [SSS]) and public health care system (Sistema Único de Saúde [SUS]).

Model Structure

Markov models have two components: structure and parameters. The "structure" refers to health states represented in the model and the possible transitions between them. The "parameters" of the model include the probabilities assigned to transitions between states of health.

To estimate costs and outcomes of each treatment, a Markov model was designed to follow patients with NVAF at risk for clinically relevant events along the natural course of the disease until the end of their lives. This model considered patients transition through different health states, as shown in Fig. 1. The primary and recurrent clinical events included were IS, hemorrhagic stroke, transient ischemic attack (TIA), systemic embolism (SE), acute myocardial infarction (AMI), intracranial hemorrhage (ICH), extracranial hemorrhage, and death. Figure 1 represents the Markov model structure with the health states considered in the analysis.

The model was evaluated within lifetime horizon (10 years). Costs and outcomes were discounted to the present value at a rate of 5% yearly, according to recommendations of the Methodological Guidelines for Economic Studies Evaluation in Health Technology Assessment, published by the Ministry of Health [10].

Patients transition through several health states has considered relevant clinical events such as IS or ICH. Depending on the event severity, patients may either return to the state they were in before the event or suffer a permanent deterioration toward a worse dependence level. In addition, patients can die as a result of a stroke or hemorrhage, or other comorbidities. A 3-month cycle duration was chosen because of the low probability for patients to have more than one severe event within this period, and it reflects the typical duration of temporary treatment discontinuation due to severe hemorrhages.

The modeling analysis allows predicting clinical and economic outcomes for a cohort of 1000 eligible patients over their lifetime, by calculating the life-years (LYs), quality-adjusted life-years (QALYs), and costs accumulated over this period depending on treatment choice. LYs are calculated on the basis of average time (in years) the patient remained alive in the model. QALY

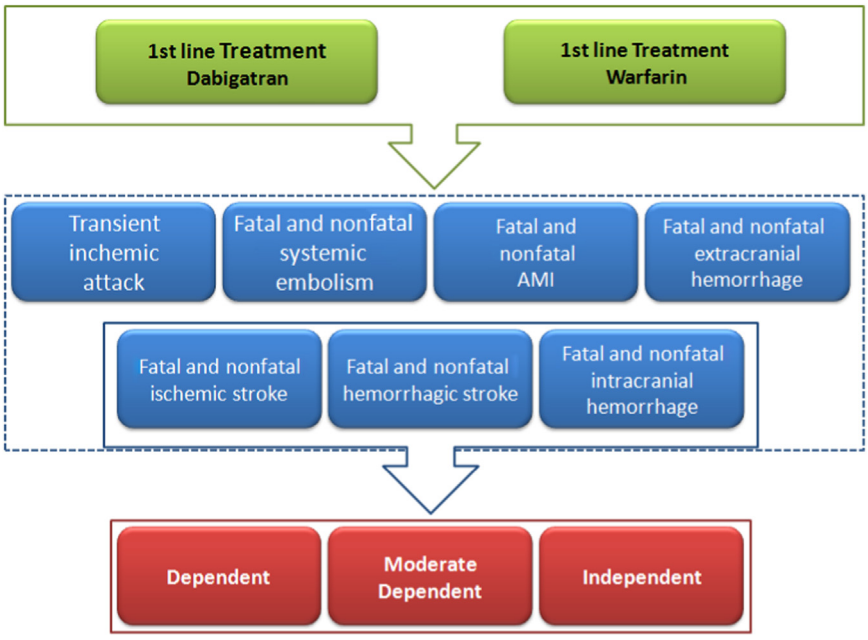

Fig. 1 – Markov model structure.