Book Chapter

Direct Oral Anticoagulants versus Warfarin in Atrial Fibrillation: An Economic Perspective

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Abstract

Background: Atrial fibrillation is a kind of supraventricular arrhythmia that impairs heart function and raises the risk of stroke. It is the most frequent arrhythmia and a significant cause of morbidity and mortality; its frequency rises with age. **Aim.** To compare the benefits versus risks of vitamin K dependent anticoagulant (warfarin) versus direct acting anticoagulants and antiplatelet therapy.

Method: Literature resources were searched to compare benefits and risks of different anticoagulants used in atrial fibrillation.

Results and Discussion: The CHADs-2-Vasc score predicts the likelihood of Stroke. Based on the assessment score, anticoagulant medication is advised. Stroke preventive medications include warfarin, dabigatran, rivaroxaban, and aspirin.

Conclusion: Rivaroxaban, and dabigatran showed superior effect and less risks of stroke incidence over warfarin in atrial fibrillation patients. Furthermore, individualized therapy selection should be based on risks and possible benefits, expense, and patient desire.

Keywords

Atrial Fibrillation; Arrhythmia; Stroke; Warfarin; Rivaroxaban; Myocardial Infarction

Introduction

Atrial fibrillation (AF) is frequent kind of heart arrhythmia. It is caused by irregular electrical activity in the heart's atria, which causes them to fibrillate. It is classified as a tachyarrhythmia, which indicates that the heart rate is frequently rapid. The arrhythmia duration may vary, which can be less than seven days (called paroxysmal arrhythmia) or more than seven days (called persistent arrhythmia). Because of the uneven rhythm, flow of blood through the heart becomes turbulent, increasing the

likelihood of the formation of a thrombus, which can eventually dislodge and lead to a stroke. [1]

The most common cardiac cause of stroke is atrial fibrillation. Advanced age, high blood pressure, existing heart and lung condition, heart defects, and increasing alcohol intake are all risk factors for atrial fibrillation. Symptoms range from asymptomatic to symptoms which include, chest discomfort, palpitations, a high heart rate, breathing difficulty, nausea, dizziness, excessive sweating, and fatigue. [1]

Since atrial fibrillation is a chronic condition, several therapies and risk-reduction approaches have been developed to assist minimize the risk of stroke in individuals who stay in atrial fibrillation. Anticoagulation therapy, rhythm control medication, ablation, cardioversion, and other interventional cardiac procedures are treatment options available for atrial fibrillation management.

Maintenance of sinus rhythm is the primary goal, especially for patients younger than 65 years with severe symptoms or first-diagnosed AF. For these individuals, restoration and maintenance of sinus rhythm may alleviate symptoms and improve the quality of life. Selection of the anti-arrhythmic drug for maintenance of sinus rhythm is based on the drug's safety and efficacy. Generally, class Ic and IIIc anti-arrhythmic drugs are mainly used for maintenance of sinus rhythm. [2]

Class Ic treatment with flecainide or propafenone is often preferred, which exerts its effects by blocking sodium channels to reduce the rate of rise of the action potential and reduce excitation of the cardiac tissue. Class Ic drugs are recommended for paroxysmal AF, but their use is contra-indicated for AF patients with underlying structural heart diseases due to increased risk of ventricular arrhythmias and atrial flutter. [3]

Class IIIc treatment with sotalol, amiodarone, ibutilide or dofetilide is often preferred, which exerts its effects by potassium channel blockade and prolonging action potential duration to delay conduction. Class IIIc drugs are recommended

for persistent AF, and also benefit AF patients with structural heart diseases. [4]

Rate-control therapy has been demonstrated to improve symptoms and reduce hospital admissions, which benefit patients older than 65 years with minimal symptoms. [5]

Commonly used drugs to control ventricular rate are β-adrenergic receptor blockers (β-blockers), non-dihydropyridine calcium channel blockers (ND-CCBs), digitalis and amiodarone. B-blockers are the preferred first-line agents for rate control during AF owing to the efficacy (lower heart rates) as well as potential survival advantage. The most commonly usedβ-blockers are metoprolol, bisoprolol and atenolol. Contra-indications should be considered before we useβ-blockers; briefly, acute pulmonary oedema, heart failure, asthma, severe atrioventricular block and severely depressed patients cannot chooseβ-blockers. [6]

Patients with AF are five times more likely to have a stroke, [7] which has long attracted the attention of clinicians. Besides, cognitive impairment, silent cerebral infarcts, memory impairment, hippocampal atrophy, Alzheimer's disease and other forms of dementia have been demonstrated at a higher prevalence in AF compared with non-AF. [8]

Anticoagulant therapy is highly recommended in preventing strokes for AF patients. Choices of anticoagulant drugs are new oral anticoagulants (NOACs), including the direct thrombin inhibitor dabigatran and the factor Xa inhibitors apixaban, edoxaban and rivaroxaban) and oral anticoagulants (OACs, such as warfarin). [2]

NOACs had a favorable risk–benefit profile, with significant reductions in stroke, intracranial haemorrhage and mortality rates, and with similar major bleeding events to warfarin. The efficacy and safety of NOACs over warfarin seem to be even greater in East Asians compared with non-Asians [9].

Combinations of OACs and platelet inhibitors increase bleeding risk and should be avoided in AF patients without another indication for platelet inhibition (Class III, level of evidence B). Aspirin is neither effective nor safe as thromboprophylaxis for AF patients, even possibly increasing stroke risk in elderly patients [10].

During anticoagulant therapy, monitoring the coagulation function is necessary to ensure the efficacy and safety of anticoagulants.

The potential benefits of novel anticoagulants come at a substantially increased cost. For example, the price of dabigatran is ≈$8 per day. Previous economic analyses suggested that dabigatran seemed to represent relatively good value for money but contained inaccuracies in the assessment of drug costs [11]. Novel agents, which act by inhibiting factor Xa or thrombin and do not require routine monitoring, may provide more consistent anticoagulation and remove the inconvenience of warfarin monitoring [12].

Two of these agents, dabigatran and rivaroxaban, are noninferior to warfarin and were approved by the US Food and Drug Administration for use in AF in October 2010 and July 2011, respectively. [13] Apixaban seems to be superior to warfarin and was approved by the US Food and Drug Administration for use in AF in December 2012 [14].

Methods

In this chapter we included data from trustable literature resources to compare benefits and risks of different anticoagulants used in atrial fibrillation. Medical subject headings (MeSH) were used for searching data. The MeSH terms of atrial fibrillation, rivaroxaban, clopidogrel, dabigatran, arrhythmia, and myocardial infarction were used to search PubMed, and MEDLINE databases. All the relevant publications up to 2022, were included.

No limits regarding study design or date were set on the search, and all studies in English language were included. The target population includes the patients who are suffering from atrial fibrillation. All studies without significant or meaningful outcomes are excluded. Duplicate records were removed. Two reviewers evaluated each search result title and abstract to determine record suitability for inclusion. The final approval was done by a third author.

Results and Discussion

Epidemiology and Risk Factors

The worldwide prevalence of atrial fibrillation (AF) is favorably associated with various areas' sociodemographic indices. Male sex, increasing age, and Caucasian ethnicity are risk factors; female sex is associated with increased atrial fibrillation mortality on global bases, most likely due to thromboembolic risk. African American, Asian, and Hispanic/Latino ethnicities, are associated with a decreased incidence of atrial fibrillation when compared to Caucasians. Atrial fibrillation may be genetic in origin, with over 100 genetic loci discovered. In the risk stratification of incident diseases, a polygenic risk score and clinical risk variables are possible and beneficial [15].

The most major risk factor for atrial fibrillation (AF) is age. It is linked to an increasing AF load, with a dramatic rise beyond the age of 65. The number of people over the age of 65 is anticipated to increase from 12 percent in 2010 to 22 percent in 2040 [16].

Numerous conventional cardiovascular risk factors were linked to atrial fibrillation incidence in both men and women, including, diabetes, hypertension, obstructive sleep apnea, and dyslipidemia. Furthermore, some life style habits may contribute in increased atrial fibrillation incidence like, sedentary behavior, obesity, sleep disturbances, smoking, and excessive alcohol consumption. Thus, therapeutic management of atrial fibrillation necessitates a thorough understanding of the patient's health status and behaviors.

Many risk factors in atrial fibrillation (AF) act throughout years. Chronic subclinical inflammation, for example, is characterized as continual low-grade stimulation of the systemic immune response. This chronic inflammation is a characteristic of biological ageing across several organ systems. On the other hand, both AF and age are linked to higher levels of reactive oxygen species. Furthermore, inflammation is linked to endothelial dysfunction, collagen catabolism, an increase in TGF-ß1 activity, and alterations in the extracellular matrix [17].

In the United States, the general prevalence of atrial fibrillation (AF) is about 1 to 2 percent. Despite a higher load of comorbidities in blacks, the prevalence and incidence of atrial fibrillation (AF) are lower in Asians and blacks than in Europeans. Possible contributing factors for that include genetic, social, and environmental health variables, which have not been well investigated. A study showed that Hispanics, Asians, and blacks over the age of 65 had 46 to 65 percent lower AF incidence than non-Hispanic whites. In research of almost 600,000 Veteran Affairs patients, whites had a nearly 2-fold greater age-adjusted prevalence of AF than other ethnicities [18].

Hypertension predisposes to cardiovascular problems such as coronary heart disease and heart failure, both of which contribute to the onset and death of AF [19]. On the other hand, diabetes is characterized by glucose intolerance and insulin resistance, both of which act as modulators of AF substrate formation [20].

Regarding smoking, it was shown that tobacco, tar, carbon monoxide, and nicotine are the most important components that cause heart diseases. Nicotine promotes profibrotic processes and inhibits potassium channels, suggesting that it may be directly implicated in the formation of an electroanatomic substrate for atrial fibrillation. Smoking indirectly increases systemic catecholamine release and promotes coronary vasospasm, which leads to myocardial ischemia and, subsequently, atrial fibrillation [21,22].
Obesity is a growing epidemic with its global prevalence doubling over the past 34 years. Based on World Health Organization global estimates, in 2014 >1.9 billion adults were

overweight. In Europe and North America, >60% of adults are overweight. A recent meta-analysis estimates a 3.5–5.3% excess risk of AF for every one unit of body mass index (BMI) increase [23].

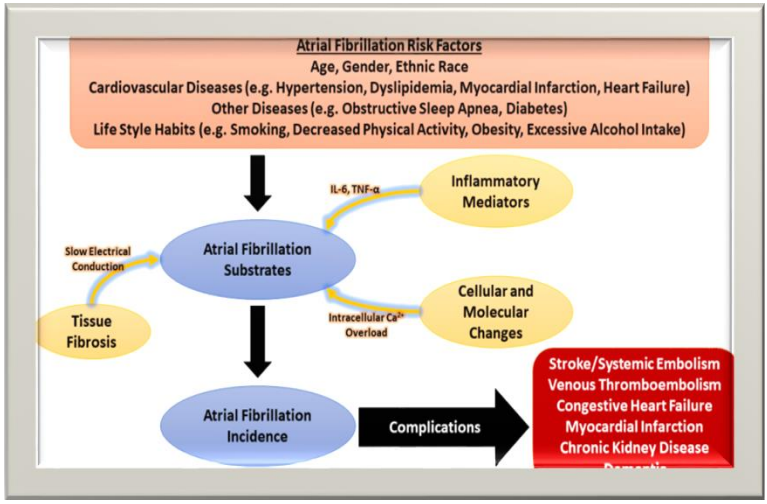

Figure 1: Atrial fibrillation (AF) risk factors. [The atrium undergoes structural and histopathologic alterations as a result of risk factors, which include fibrosis, inflammation, and cellular and molecular abnormalities. Such alterations make people more susceptible to AF. Persistent AF also causes electric and structural remodeling, which favors the continuation of AF].

Atrial Fibrillation Comorbidities and their Prognosis

Atrial fibrillation (AF) is linked to an increased risk of death. Patients often die from comorbidities and consequences, such as heart failure (HF), myocardial infarction (MI), chronic kidney disease (CKD), venous thromboembolism (VTE), stroke, dementia, and malignancy, rather than the arrhythmia itself. Aside from similar risk factors, AF and associated comorbidities have a number of direct causative connections [24].

Heart failure (HF) and atrial fibrillation (AF) are closely connected, and their coexistence is related to significantly increased morbidity and death. Atrial fibrillation and heart

failure are linked to an increased risk of other disease conditions, implying a bidirectional association. A study showed that 37% of the participants who developed new AF had previously been diagnosed with HF. On the other hand, 57% of persons developing HF had prevalent AF [25].

The risk of myocardial infarction (MI) is nearly doubled in persons with atrial fibrillation (AF). In contrast, MI is associated with an increased incidence of AF, particularly in the acute phase. The coexistence of MI and AF is linked with a 40% increase in mortality [18].

Higher atrial fibrillation (AF) incidence is correlated with albuminuria, moderate renal impairment, and deteriorating renal function. Patients with a glomerular filtration rate of 30 to 59 mL/min were 32% more likely to have AF than those with normal renal function. Furthermore, the risk was 57% greater for individuals with a glomerular filtration rate of less than 30 mL/min than those with normal renal function [26].

New-onset AF is prevalent following cardiac surgery, affecting 20-40% of patients admitted for coronary artery bypass grafting operations, but it was previously thought to be of little long-term prognostic significance [27].

Value-based Healthcare: Concept, Implementation, and Challenges

There have been numerous initiatives over the past century to increase care while reducing societal expenditures. The need for care has grown as a result of longer life expectancies, advancements in technology, and more knowledgeable people. But despite the higher investment, healthcare institutions are having trouble meeting the rising demand [28,29]. Despite attempts to improve care while reducing costs have resulted in an explosion of approaches and strategic frameworks, no consensus on what it means to "improve" care. One of these strategies has been termed value-based healthcare [30].

Value in healthcare refers to the cost of improving a patient's health outcomes to the measured improvement [31]. The transformation to value-based care aims to give the healthcare system the ability to add greater value for patients. Descriptions of value-based health care that focus on cost reduction are insufficient because the value is only established when a person's health outcomes improve. Cost-cutting measures are crucial, yet they fall short [32].

Stakeholders in the health care system, such as patients, providers, health plans, employers, and government agencies, share the goal of enhancing patients' health outcomes in relation to the cost of care. Value-based healthcare is so well-aligned with the objectives of these many groups that, soon after the idea was floated in 2006, health economist Uwe Reinhardt called it "a utopian vision". While acknowledging the difficulties of switching to a value-based system, Reinhardt praised the transformation's wider goals [33].

Value-based healthcare is sometimes conflated with quality, a nebulous notion that suggests a variety of values and frequently focuses on inputs and process compliance in the healthcare industry. However, while using comparable techniques, the outcomes of different teams' quality improvement efforts can differ. Furthermore, mandates for monitoring and reporting procedure compliance may divert caregivers from the more important objective of enhancing health outcomes [34].

The fact that a patient's perspective of value is complex and that different patients may assign various weights to different aspects or traits presents a significant challenge for managers and policymakers in operationalizing value-based healthcare. Patients' expectations, which are influenced by a variety of personal circumstances, will play a part in how they perceive the value [35].

The following factors may be present in some or all of a patient's perspective: 1) clinical outcomes of care, such as complication rates; 2) patient-reported outcomes of care, such as pain relief and improved mobility; 3) patient experience of care, including

issues of being treated with dignity, privacy, cultural appropriateness, and continuity of care; 4) access to care issues, including waiting times; and 5) patient cost of care [36].

These dimensions will carry varying weights with various persons. Patients will differ depending on their pain tolerance and some people will be surgery averse and place a high value on guidance and reassurance while others will be highly concerned about out-of-pocket costs. One of the reasons it is challenging to turn the value-based, patient-oriented hype into real policy is the multiplicity of patient perspectives [37].

Decision-makers frequently combine the views of quite different types of patients when determining the priorities and resources to be allocated across the entire system. For instance, the widely varied valuations in heterogeneous populations will be lost if the out-of-pocket payments of patients who are wealthy and those who are poor are combined into a single average. In other words, decision-makers frequently make assumptions away from the distribution and believe that the average experience sufficiently represents the entire population [36].

Although the macro level of operationalizing value-based care poses some challenges, recognizing at the level of service delivery individual differences in patients' perceptions of value and how patients may perceive the healthcare system differently due to their race, income, gender, or sexual orientation would be advantageous for everyone, but especially for vulnerable groups [38].

Because existing atrial fibrillation (AF) pattern-based classifications are empirical, their accuracy and reliability are doubtful. The typically fleeting and changeable character of atrial fibrillation limits clinician-guided, pattern-based categorization and makes AF classification difficult. Evidence shows that atrial fibrillation incidents are commonly asymptomatic, that symptoms do not consistently indicate AF episodes, and that long-term surveillance uncovers previously unreported AF events [39].

The previous challenges in atrial fibrillation classification in turns lead to lack of proper medical care. The net results will be an increased potential disease risks and complications, and so increased disease treatment cost.

An investigation done in Europe showed that in the United Kingdom, apixaban, rivaroxaban, and dabigatran are cost-effective alternatives to Vitamin K antagonists anticoagulants. On the other hand, the results in Netherlands showed that only apixaban and dabigatran are cost-effective. It seems that the new oral anticoagulants' cost effectiveness is heavily influenced by the location and quality of local anticoagulant care facilities [40].

Management of Atrial Fibrillation and (Direct anticoagulants versus warfarin)

The treatment of acute atrial fibrillation is dependent on hemodynamic stability and risk classification. In circumstances when the patient is hemodynamically unstable, urgent cardioversion with anticoagulant medication is suggested. Although a transesophageal echocardiography (TEE) is suggested before any cardioversion, it may be necessary prior to TEE if the patient is hemodynamically unstable due to a fast ventricular response [1].

A beta-blocker or calcium-channel blocker should be started for rate control if there is evidence of fast ventricular response. These choices are available in intravenous (IV) form for quick response. If symptoms do not improve after an IV bolus, the patient is generally placed on a drip. Digoxin can be used for heart rate control; however, it is not recommended as a first-line treatment due to its adverse effects and tolerance. Amiodarone can also be used as a rhythm control drug; however, it is not a first-line choice in an emergency setting. In any event, if the choice to begin amiodarone is taken, cardiologist should be contacted before starting it [1].

The meta-analysis in a systematic review showed that DOAC use was associated with a significantly lower risk of stroke (as indicated in 6 studies, included 7143 patients) than warfarin, a

tendency toward lower risk of systemic embolization (4 studies, 7289 patients), and similar risks of bleeding (14 studies, 10182 patients) and mortality (12 studies, 9843 patients). Current data demonstrates that DOACs, when compared to warfarin, are linked with a decreased risk of stroke and a significant tendency for a lower risk of systemic embolization, with no indication of increased risk for hospital readmission, bleeding, or death [41].

A clinical study included 439 persons with bioprosthetic heart valves (BHCVs) and atrial fibrillation (AF) were given a DOAC, while 2233 were given warfarin. The findings indicated that there was no significant difference in usage of DOACs against warfarin for the key effectiveness outcome of ischemic stroke, systemic embolism, and transient ischemic attack ($p = 0.11$). DOAC use was linked to a decreased risk of the key safety endpoint of cerebral hemorrhage, gastrointestinal bleeding, and other bleeding (p 0.001). which means that these data support the use of DOACs for AF in BHV patients [42].

The CHADs-2-Vasc score, which is useful in calculating the risk of stroke every year, should be used to stratify the patient risk. Based on the risk assessment findings, clinicians should consider anticoagulant and/or antiplatelet medication [43].

Table 1: Comparison between different direct acting anticoagulants, antiplatelet agents and warfarin.

Drug	Warfarin	Rivaroxaban	Dabigatran	Clopidogrel
Mechanism of action	Competitive inhibitor of vitamin K epoxide reductase complex 1 (VKORC1) which is an essential enzyme for activating the vitamin K. So, warfarin can deplete functional vitamin K reserves and thereby reduce the synthesis of active vitamin K-dependent clotting factors [44].	Targeting free and clot-bound Factor Xa and Factor Xa in the prothrombinase complex [45]	Reversibly binding to active site on the thrombin molecule. Preventing thrombin-mediated activation of coagulation factors [46]	By blocking the adenosine diphosphate receptor and subsequent activation of the complex IIb/IIIa, clopidogrel prevents platelet aggregation [47].
Indication for use	Atrial fibrillation Venous thromboembolism Prosthetic heart valves [48].	Prevention of venous thromboembolism (VTE) in patients undergoing hip or knee replacement surgery. Long-term prevention of stroke in patients with non-valvular atrial fibrillation Long-term secondary prevention of recurrent VTE [49].	Prevention of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF) [50]	Management of unstable angina (UA) in patients receiving fibrinolytic therapy non-ST-segment elevation myocardial infarction (NSTEMI) in patients receiving fibrinolytic therapy ST-segment elevation myocardial infarction (STEMI) in patients receiving fibrinolytic therapy. Secondary prevention in recent myocardial infarction (MI) Secondary prevention in recent stroke, and peripheral arterial disease. [51]
Potential associated risk	Bleeding and significant hemorrhage (e.g, intracranial hemorrhage, gastrointestinal (GI) bleed, hematemesis, intraocular bleeding, hemarthrosis). [52] Drug interaction: NSAIDs, aspirin, or macrolide antibiotics, are associated with increased bleeding risk [53].	Patients receiving rivaroxaban for any therapeutic indication have a lower risk of intracranial bleeding compared to patients receiving vitamin K antagonists alone or in sequential treatment with low-molecular-weight heparins [54]. Drug interactions: Amiodarone, Fluconazole, Phenytoin, Aspirin, NSAIDs, are associated with increased bleeding risk [55].	When compared to warfarin, dabigatran had a reduced risk of cerebral hemorrhage but an increased risk of significant gastrointestinal (GI) bleeding. [56]	Dual therapy of aspirin and clopidogrel is a risk factor for both major and any bleeding [57]. The hemorrhagic risk associated with warfarin therapy combined with antiplatelet therapy appears to outweigh the benefits. A study found that patients who received combined anticoagulation and antiplatelet therapy were 2.75 times more likely to experience a clinically significant hemorrhage. [58]

Advantages	Warfarin is effective in both primary and secondary stroke prevention in individuals with atrial fibrillation, with 60 to 70% relative decrease in stroke risk compared to placebo and 26% reduction in death rates [59].	Body weight has no effect on the pharmacokinetic profile of rivaroxaban. According to research study, people on rivaroxaban had a 26% reduced risk of stroke or systemic embolism than those taking warfarin [60]. Rivaroxaban could be superior over warfarin in atrial fibrillation patients that encounter covid-19 infection [61].	Dabigatran etexilate 150 mg twice daily is more effective than warfarin in preventing stroke and systemic embolism in patients with atrial fibrillation Dabigatran is typically well tolerated, especially in terms of bleeding endpoints when compared to warfarin. [62]	In patients with coronary stents, the combination of aspirin and clopidogrel is more effective than oral anticoagulants [63].

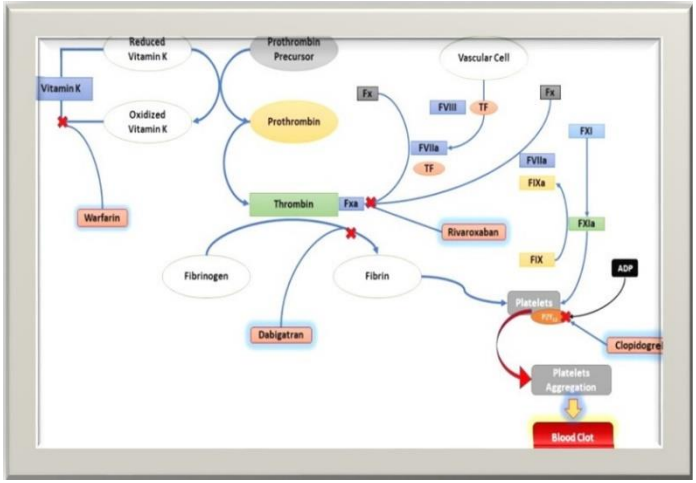

Figure 2: Mechanism of action of warfarin, dabigatran, rivaroxaban, and clopidogrel. [Warfarin interferes with vitamin K cycle. It binds to oxidized vitamin K reductase enzyme, so that it cannot be recycled. The lack of reduced vitamin K limits the carboxylation of coagulation factors such as prothrombin precursor. Dabigatran targets thrombin directly, while rivaroxaban target factor Xa. Clopidogrel inhibits the binding of adenosine diphosphate (ADP) to its platelet P2Y12 receptor, and so prevent mediated ADP activation of platelet aggregation].

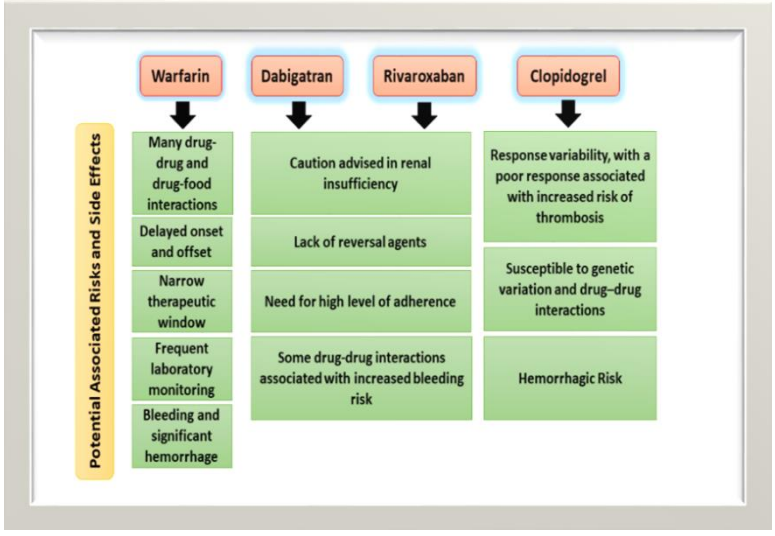

Figure 3: Potential risks and side effects of warfarin, dabigatran, rivaroxaban, and clopidogrel.

Direct Oral Anticoagulants versus Warfarin in Atrial Fibrillation: An Economic Perspective

Guidelines in Europe and the USA indicate preferential use of DOACs over warfarin to prevent cardiovascular problems in patients with AF, based on growing evidence that DOACs are more cost-effective than warfarin [64,65]. The incremental cost-effectiveness ratio (ICER), however, is controversial; it can be negative due to an intervention's lower cost but higher efficacy or higher cost and lower effectiveness. Recently, a novel strategy has been proposed, involving the conversion of incremental cost-effectiveness ratio (ICER) to incremental net benefit (INB), then pooling the INB across studies (i.e, a positive INB indicated favor the intervention) [66].

A systematic review and quantitative meta-analysis by Noviyani et al [67], has included a total of 100 eligible economic evaluation studies (224 comparisons) that were conducted in various healthcare settings to guide health policymakers in relation to the reimbursement of DOACs for stroke prevention in AF. The authors pooled INBs associated with four DOACs (dabigatran, apixaban, rivaroxaban, and edoxaban) across studies; stratified by level of country income, time horizon, perspective, and model types. The study's findings indicated that while DOACs were not more cost-effective, at their current pricing, in upper-middle-income countries regardless of the perspective employed, DOACs may be significantly more cost-effective than VKAs in high-income countries when using the perspective of third-party payers.

However, only dabigatran remained cost-effective compared with VKAs from a societal perspective. The results also showed that the country’s socioeconomic status and the methodology employed may have had an impact on the cost-effectiveness of DOACs in comparison to VKAs. Pharmaceutical companies and policy makers should together consider potential pathways to increase patients’ access to these agents by considering the impact of socioeconomic status on the cost-effectiveness for upper-middle-income countries and potentially low-income and middle-income countries [68].

Cost effectiveness of direct oral anticoagulants like dabigatran may contribute in decreasing the economic burden on healthcare systems and families. Furthermore, it will increase the patient treatment compliance and therefore, decrease potential associated disease risks, and improve patents' quality of life.

Should we Screen for Atrial Fibrillation?

Paroxysmal AF, as opposed to persistent AF, affects about 25% of patients with AF [69]. The percentage of time a patient spends in AF, is referred to as the AF burden which appears to be a significant component in predicting the risk of stroke, despite the fact that risk prediction tools do not take this into account. Even after controlling for important factors including age and sex, a systematic review by Ganesan et al. revealed that persistent and permanent AF were linked to a higher risk of thromboembolism and all-cause mortality compared to paroxysmal AF [70].

Extended screening can detect brief episodes of paroxysmal AF and atrial arrhythmia using devices like pacemakers, patches, implanted cardiac monitors, or smartphones. Those who have implanted cardiac devices frequently experience these episodes. However, the clinical significance of brief short episodes of arrhythmia remains uncertain although different durations of arrhythmia have been identified to differentiate such episodes and AF from electrical artefacts. Currently, the detection of the typical arrhythmia for at least 30 s is required for the diagnosis of AF [71].

Patients with AF diagnosed with a single ECG cannot be stratified based on their AF burden. In the setting of extended monitoring, stroke risk scores have not been validated for AF diagnosed to help determine if anticoagulation will be of net benefit. Even those with very low AF burdens would be recommended treatment if current guidelines were applied to AF identified through extended screening [72]. In these circumstances, the risk of bleeding from anticoagulation may outweigh the reduction in stroke risk [71].

Systematic opportunistic screening is thought to be more cost-effective compared to a systematic population screening program [73,74]. A systematic approach may be cost effective within 3 years as proposed by the cost-effectiveness analysis of STROKESTOP [71]. Moreover, the efficiency of systematic AF screening could be maximized by targeting individuals at higher risk of incident AF [76].

From another angle, to provide coordinated treatment and follow-up, any nationwide screening program would need new management pathways tailored to each individual country. This would have enormous financial ramifications for the program infrastructure, the screening tools, and the medical care. However, spending money on enhancing and standardizing current AF management may be more beneficial [71].

Anticoagulation rates around the world are consistently below target levels [77]. Over 22% of the 94,000 patients in the Riks-Stroke registry who experienced an ischemic stroke had previously been diagnosed with AF, yet only 16% of these had been prescribed anticoagulation in the six months before their stroke. Anticoagulation prescribing was inversely correlated with risk score, thus people at higher risk were less likely to receive treatment [78]. Anticoagulation is cost-effective for preventing strokes, as has been shown, and suboptimal anticoagulation prescribing in high-risk patients has a considerable economic impact [79,80].

Future research may show that AF screening reduces the risk of stroke, but it will still be necessary to compare its cost-effectiveness to other programs designed to enhance anticoagulant dosing [71]. Lately, evidence is growing that, when paired with rhythm monitoring in a clinical research, prediction models developed using artificial intelligence in routinely collected electronic health records can provide good discriminative performance for AF and enhance detection rates [81].

Standardizing atrial fibrillation stratification and enhancing its identification methods may be more beneficial and cost effective

besides current atrial fibrillation screening methods. The early, precise, and accurate identification of atrial fibrillation episodes will contribute in avoiding possible disease complications that result from non-treating the disease or improper medication.

Conclusion

Anticoagulation is an effective treatment for stroke prevention in patients with atrial fibrillation (AF). However, direct acting anticoagulant like rivaroxaban, dabigatran showed superior effect and less risks of stroke or systemic embolisms incidence over vitamin K antagonist, warfarin in atrial fibrillation patients. Furthermore, clopidogrel showed to be more effective in combination with aspirin in patients with stents over other anticoagulants.

Recommendations

Rivaroxaban, and dabigatran is highly recommended as first line choices in management of atrial fibrillation. However, individual investigation for each patient case is recommended before therapeutic choice decisions.

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