Global Perspectives

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THE QUEST TO PREVENT STROKE IN ATRIAL FIBRILLATION: FIGHTING THE FLUTTERING HEART IN SINGAPORE

There has been resurgence in the attention placed on pharmacotherapy in atrial fibrillation (AF) recently as specialists in international conferences discuss the utility of novel anticoagulants with caution owing to limited knowledge of the side effect profile in this nascent stage. AF is a well-known risk factor for stroke and has been for more than 20 years, since warfarin was demonstrated to reduce the risk of stroke, with aspirin doing so to a lesser degree.[1] Today, there is international variation in the use of warfarin to prevent stroke despite well-established data.[2] Singapore finds itself in a peculiar geographical and clinical position.

Risk–treatment disconnect. A Chinese idiom quoted frequently explains that if one knew the enemy as well as oneself, a hundred out of a hundred battles would be won. The frustration in AF is 2-fold. The first is that it is underreported. Paroxysmal AF is known to render the same risk of stroke as nonparoxysmal AF, yet due to its transient nature the former is not always detected. Second, known AF is undertreated, with a risk-treatment disconnect.

We have identified this problem of underuse of anticoagulation in our local study of patients admitted to a tertiary institute with a first ischemic stroke. The majority of those admitted with AF were individuals with known AF. Even though all of these patients had intermediate to high risk of stroke based on CHA2DSVASC2 scoring, only 1 person (1.6%) was therapeutically anticoagulated on admission. In Singapore, untreated AF is a significant risk factor for stroke.

Low rates of anticoagulation in the region. This clinical situation in Singapore is peculiar—it may be typical of countries in this region, yet it is also unexpected given the affluence of the society. The rate of anticoagulation with warfarin in patients with AF from 44 countries (in Europe, North and South America, and Asia) has been reported to be 53%.[3] The figure illustrates that the rate of anticoagulation is lower in countries in Southeast Asia (SEA) and Latin America.[2] In SEA, the rate of anticoagulation varies between 25.5% and 52.9%. Singapore had a rate of 35.8%.

We are in a region that is reluctant to prescribe anticoagulation. It is thought that adherence to therapy is hampered by poor access to care and limited resources required for frequent monitoring of patients to ensure a therapeutic international normalized ratio (INR). Yet this is unexpected as Singapore has different circumstances. We have accessible health care in a small, urban city-state and a literate population that should understand the benefits of warfarin.

Evidently, underuse of anticoagulation is a complex problem that requires further qualifying—whether it is due to hesitant physicians or disagreeable patients. We are in a cultural landscape where what is practiced as evidence-based medicine is still thought to be "Western" medicine that has to be accepted slowly. It has to be rationalized with traditional medicine even in Singapore, and especially in rural communities.

Challenges ahead. The above findings have caught the attention of local neurologists and cardiologists alike. Qualitative analysis of reasons why these patients are not anticoagulated is needed to facilitate enabling factors and remove barriers to treatment. One enabling factor is the minimization of the logistical difficulty of dose titration. To facilitate a high turnover of patients on follow-up for warfarin titration, there are anticoagulation clinics designed to service a high volume. Charts that determine the exact changes in doses required for a particular weekly dosage regimen based on the INR on arrival are readily available in clinics.

Moving forward, there is ongoing research in devising a pathway that standardizes how investigation and treatment of AF is managed when first picked up by physicians. A discussion of risks and benefits of anticoagulation can be made at that point, personalized to the patient's current functional status and comorbidities. It is important to ensure when and at what intervals anticoagulation is offered depending on whether a first stroke is massive or disabling, the bleeding risks, and the functional independence of the patient.

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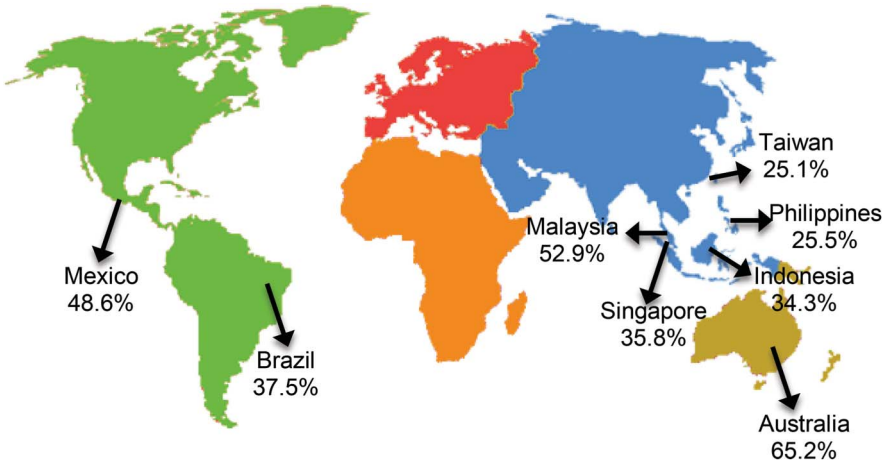
Figure International variation in the rates of anticoagulation



World map shows that rates of anticoagulation vary across regions and are particularly low in Southeast Asia and Latin America.

In time, we hope to reap the benefits of novel anticoagulants (NOAC), which are used by a minority of the AF population. While promising in convenience of administration, these drugs are not popular. In a country that subsidizes the cost of mainly "common" drugs for chronic diseases, the NOAC are considered nonessential and are costly to the patient, costing $7 SGD per day instead of $0.12 SGD (the cost of warfarin). In addition, some local physicians are reluctant to advocate the drug because of unfamiliarity with the pharmacokinetics of the drug and with the management of bleeding episodes. As yet, there is no antidote available for rivaroxaban or dabigatran, and the absence is palpable.

The health care funding system should be renewed to subsidize NOAC due to the potentially low incremental cost-effectiveness ratio. NOAC give us the opportunity to prevent strokes in patients who are not suitable for warfarin but who are otherwise candidates for anticoagulation, hence the increase in quality-adjusted life-years is significant. There is emerging evidence that NOAC are cost-effective alternatives to warfarin.[4] Prevention is economical as every incident stroke imposes a heavy burden on the health care system due to a hefty lifetime cost that is easily underestimated when 58% of it is indirect.[5]

The benefit of an enabling new pathway or policy to increase anticoagulation rates can only be seen in years to come. In the immediate phase, it is essential to address existing barriers to treatment—there is a culture of reluctance to take "blood thinners" in societies still reliant on traditional medicine. Patients need to know that compared with purported nonspecific health benefits of traditional medicine, the known stroke risk reduction of warfarin is a more promising prospect. Many fear a dramatic bleeding complication, yet a thromboembolic phenomenon may be much more catastrophic. These myths can be debunked through conscientious public health campaigns and with a multidisciplinary approach. In practice, pharmacists have multiple points of contact with patients when counseling them and dispensing medication. Collectively, we will be able to inform individual patients better on the truths of anticoagulation.

Physicians play a key role in ensuring appropriate anticoagulation in AF. Nonstroke specialists are more inclined to make a value judgment of suitability of a patient for anticoagulation based on a memory of the last bleeding complication encountered. Yet it is difficult to perceive the benefit of a stroke prevented. Sick patients present to the hospital; well patients do not. In situations where anticoagulation is indicated and offered, there is no room for ambiguity in explaining to patients the certain benefit of anticoagulation and lack of known benefit of a traditional alternative. Professional seminars and updates must emphasize to physicians the strong data that risk stratify AF and support the use of anticoagulation so that they will be disciplined in offering appropriate anticoagulation. The cultural barriers mentioned above should be highlighted so physicians can address these concerns with the patients specifically and give them time to clarify the meaning of competing risks and benefits of one treatment.

For all patients with AF, each successfully conducted electrical activity has potential to cause a debilitating stroke. Whether a clot will be thrown off is as unpredictable as, and intricately linked to, the onset of the next heartbeat. Thus it is with urgency that we seek to improve the current treatment of AF.

AUTHOR CONTRIBUTIONS

Dr. Orlanda Goh: drafting/revising the manuscript, study concept and design, analysis and interpretation of data, acquisition of data, statistical analysis. Dr. Gillianne Lai: revising the manuscript. Dr. Tian Ming Tu: interpretation of data, acquisition of data, study supervision and coordination. Dr. Kim En Lee: study concept and design, interpretation of data, acquisition of data, study supervision and coordination.

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DISCLOSURE

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