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THE PATTERN USE OF ANTI-THROMBOTIC IN ATRIAL FIBRILLATION PATIENTS IN SOUTHEAST ASIA: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Stroke prevention in AF patients is a very important. One of therapeutic goals is prevention of thromboembolism with anticoagulation. there has been very limited data on pattern of use of antithrombotic therapy for atrial fibrillation patients in southeast Asia. **Aim:** review the use of antithrombotic therapy pattern for ischemic stroke with atrial fibrillation in in southeast Asia**. Methods:** We performed a comprehensive search on topic that the pattern of anti-thrombotic use in atrial fibrillation patients with in southeast asia from inception up until November 2019 through PubMed, and Cochrane Central Database. Systematic research process was using various keywords. The keywords were: "anti-thrombotic", "anti-coagulation", and "atrial fibrillation', The operator "and" was then used with the name of each country in southeast Asia. The inclusion criteria of the study i.e: patients with AF, was a original papers with observational study, concerned on use of anticoagulation in patients with atrial fibrillation in southeast Asia. **Results:** Data of using antithrombotic are available in six countries in southeast Asia, a total of the 8 articles identified were from Philippine, Thailand, Vietnam, Singapore, Indonesia, and Malaysia were also represented. The reported The rate of using Anticoagulation for secondary prevention of stroke in southeast Asia is ranged 7.7% to 18.2%. **Conclusions:** The rate of using Anticoagulation for secondary and primary prevention of stroke in southeast Asia is still low. The Pattern Use of antithrombotic in Stroke Patients with Atrial Fibrillation showed that warfarin is the most widely used Anticoagulation in southeast Asia countries.

KEYWORDS: Stroke prevention in AF patients is a very important.

1. BACKGROUND

Atrial fibrillation is the common cardiac arrhythmia in clinical practices which is an important health care issue and a major cause of morbidity and disease worldwide.[1] This disease burden due to AF is rapidly increasing, especially in Asia, including southeast Asia countries.[1,2] According to the consensus of the Asia Pacific Heart Rhythm Society on stroke prevention in atrial fibrillation. the number of patients AF in Asia is expected to reach 72 million in year 2050.[3]

AF is associated with a higher risk of recurrent stroke and greater mortality.[1,2] Patients with AF have a five-fold risk of stroke in comparison to that of patients without AF.[4] Asian population was reported to have a higher risk of tromboembolism event compared to Western population.[5] Therefore stroke prevention in AF patients is very important. One of therapeutic goals is prevention of thromboembolism with Anticoagulation.[1]

Warfarin is the most effective Anticoagulation for prevention of thromboembolism in AF.[1,2] However In previous study, the benefit of warfarin for stroke prevention in patients with AF was offset by the risk of bleeding.[2,5] In this era of non-vitamin K antagonist oral Anticoagulation with low bleeding profiles, we can expect a more effective for primary and secondary prevention of stroke by selective anticoagulation.[5] there has been very limited data on patterns of use of antithrombotic therapy atrial fibrillation patients in southeast Asia via the analysis of real-world data in this era. The purpose of this study is to review the use of antithrombotic therapy pattern for ischemic stroke with atrial fibrillation in southeast Asia.

2. Methods

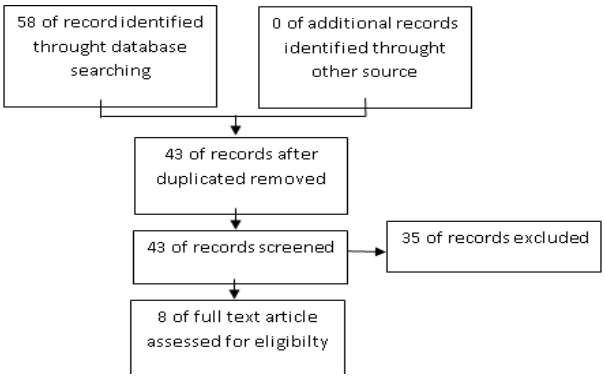

Figure 1: Flow diagram.

We performed a comprehensive search on topic that the pattern of anti-thrombotic use in atrial fibrillation patients with in southeast Asia from inception up until November 2019 through PubMed, and Cochrane Central Database. Systematic research process was using various keywords. The keywords were: "antithrombotic", "anticoagulation", "atrial fibrillation', was then used with the name of each country in Southeast Asia. The inclusion criteria of the study i.e : patients with AF, was an original paper with an observational study, concerned on the use of anticoagulation in patients with atrial fibrillation in southeast Asia. All the data search was conducted by a single author (RP) We include all related clinical researches/original articles including conference proceedings and exclude case reports, review articles, and non-English language articles Guideline selection process summarized in figure 1.

Table 1: Characteristics of the observational studies on atrial fibrillation in southeast Asia.

Research site	Publication year	Age	Sample	Anticoagulation	Antiplatelet	Antocoagulant + Antiplatelet	
Philippine	2014[6]	40-50 (35%)	40	**Valvular-AF**: Warfarin (80.9%) **Non valvular - AF**: Warfarin (42.1%)	**Valvular-AF:** Aspirin (9.5%) Aspirin and Clopidogrel (9.5%) **Nonvalvular-AF:** Aspirin (15.8%) Aspirin and Clopidogrel (10.5%)	**Non-valvular AF**: Aspirin and Warfarin (5.3%)	Primary Prevention
Thailand	2014[7]	>65	-	Anticoagulation therapy (89.9%)	Antiplatelets (19.6%)		Primary Prevention
Thailand	2018[8]	67.3 ± 11.3	3218	Anticoagulation (66.0%): Warfarin (90.9%) DTI (3.3%) Factor Xa inhibitors (5.8%)	Antiplatelets (17.3%)" Aspirin (88.0%) ADP/P2Y12 inhibitors (22.2%)	Antiplatelet and Anticoagulation (26.5%)	Primary Prevention
Vietnam	2016[9]	76.2±8.9	461	Anticoagulation (22.2%)			Primary Prevention
Singapore	2015[10]	69.8±13.3	163	Warfarin (35%)			Primary Prevention
Singapore	2016[11]	67.2 ±14.4	1095	Warfarin (32.2%)	Antiplatelet (62.5%)		Primary Prevention
Indonesia	2018[12]	>40	77	Anticoagulation (7.7%)	Antiplatelet (92.2%)		Secondary Prevention
Malaysia	2016[13]	71.0 ± 2.2	207	Anticoagulation (18.2%)	Aspirin (18.2%)		Secondary Prevention

3. RESULT AND DISCUSSION

Data on using antithrombotic in AF patients are available in six countries in Southeast Asia, a total of the 8 articles identified were from Philippine, Thailand, Vietnam, Singapore, Indonesia, and Malaysia were also represented. It is common that AF is combined with stroke. AF is one of the poor prognosis factors in patients with stroke and becomes one of the risk factors for stroke. Asian patients had a higher risk of stroke or transient ischaemic attack than non-Asians.[14] Oral Anticoagulation is recommended for primary and secondary prevention stroke in patients with AF. Current practice guidelines recommend the use of Anticoagulation in patients with AF that have risk factor according to CHA2DS2VASc score for primary prevention of stroke and Time of Anticoagulation use in post-stroke to prevent recurrent stroke according to the severity of stroke by NIHSS.[1]

Anticoagulation is the most important intervention to the prevention of stroke in patients with atrial fibrillation (AF). Two studies in Indonesia and Malaysia revealed that the rate of using anticoagulation was 7.7% and 18.2% for patient AF after the stroke event. Similar to the previous study that In Asia the rate of oral anticoagulation use was lower compared to in Europe in

hospital-based studies.[15,16] The use of Anticoagulation therapy varied widely among countries in patients with AF in southeast Asia (0.5%-20%).[17,18] Although ESC Guideline recommended to initiate anticoagulation in all AF patients between 1 and 12 days after an ischaemic stroke, depending on NIHSS (stroke severity).[1]

For primary prevention, Thailand was the highest country of using Anticoagulation therapy (89.9%), on the other hand, Vietnam was the lowest country of using Anticoagulation therapy (22.2%) in the hospital-based study. Using Anticoagulation for primary and secondary prevention is prescribed to be lower in Southeast Asia Countries than in European countries (91.1%).[16] In Review, Aspirin still is prescribed for primary prevention ranged from 9.5% to 62.5%.[19] Thus, Using Antiplatelet agents for primary stroke prevention in Asian AF patients is overused, in whom these drugs are not effective for primary prevention. Antiplatelet therapy was common in Asia (25.0%) and least prevalent in Europe (6.0%)[19] In southeast asia, The rate of patients using antiplatelet therapy was 18%–58%.[17]

Warfarin is anticoagulation that frequently used for primary prevention in AF patients in the southeast countries. The most common country is Thailand which uses this type of Anticoagulation for primary prevention in non-valvular AF patients. this study from a multicenter registry in patients with AF founded that a rate of Anticoagulation use was 66.0% for primary prevention of stroke. Among those who received Anticoagulation, 90.9% used warfarin and 9.1% used NOACs include DTI (3.3%) and Factor Xa inhibitors (5.8%)[8] Similar to Singapore and Philippine that frequently use Warfarin. In Philippine, Warfarin is highly prescribed for valvular AF.[6] In patients with significant mitral stenosis or mechanical valves with Atrial Fibrillation, warfarin is the treatment choice.[1] Warfarin is an unpredictable drug in particularly high-risk of hemorrhage.[11] Asian individuals had a higher risk of side effects Anticoagulation hemorrhagic stroke than other countries. Warfarin had the limitation that it is influenced by many diets and patient factors it can be difficult to achieve good anticoagulation control.[20]

Different from Warfarin had a big challenge of a bleeding event, NOAC drugs give a solution to this challenge.[21] Currently, NOACs have been approved for primary and secondary prevention in patients with AF. Direct thrombin inhibitor (3.3%) and Factor Xa inhibitors(5.8%) were prescribed in Thailand .8 NOAC rarely use in southeast country, however, the previous study showed that NOAC have better outcomes in fewer hemorrhagic strokes compared than warfarin.[3] NOAC have demonstrated superiority to warfarin in the prevention of stroke and the drugs are significantly associated with lower incidence of hemorrhage than warfarin.[21] European Society Congress (ESC) 2016 demonstrated that the use of NOAC for stroke prevention in AF patients has been recommended as a new standard and preferred treatment in comparison with vitamin K antagonists (warfarin).

Generally, NOAC has comparable efficacy and superior safety, compared with warfarin.[21] However, every NOAC has different pharmacokinetic, pharmacodynamics, drug interaction, and efficacy and safety profiles.[22] Therefore CHAD-VAS score, age, comorbidity, concomitant drugs, and patient lifestyle should be considered for decision NOAC's dosage.[23] Primary and Secondary prevention for stroke is important factors, Some studies have shown promising results on NOACs in patients with end-stage renal disease. The most important anticoagulation should be individualized according to individual stroke risk and bleeding risk in a patient with AF.[21]

4. CONCLUSIONS

The rate of using Anticoagulation for secondary and primary prevention of stroke in southeast Asia is still low. The Pattern Use of Anti-thrombotic in Stroke Patients with Atrial Fibrillation showed that warfarin is the most widely used Anticoagulation in southeast Asia countries, although the Asian population had a higher risk to bleeding than other population. The using novel drug, NOAC, is still limited for treatment on the other hand NOAC are superior to warfarin for stroke prevention in AF, and are associated with a reduced incidence of hemorrhagic stroke and intracranial hemorrhage compared with warfarin.

Disclosure

No conflict of interest.

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