Fact-finding survey of antithrombotic treatment for prevention of cerebral and systemic thromboembolism in patients with non-valvular atrial fibrillation in 9 countries of the Asia-Pacific region

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Atrial fibrillation (AF) has been gaining much attention as one of the major causes of cerebral infarction. It is imperative to establish antithrombotic treatment for AF patients. Thus far, guidelines for antithrombotic treatment in the management of AF patients, including the verification of the efficacy of direct thrombin and factor Xa inhibitors, have been published from the United States, Europe, Canada, and Japan. When we look at the Asia-Pacific region, antithrombotic treatment has not yet been defined, and no such guidelines have been published in this regard. The Asia-Pacific Heart Rhythm Society (APHR Society) conducted a Web-based survey between June and August 2011, to elucidate the current status of antithrombotic treatment in 9 countries.

A total of 363 cardiologists in 9 countries examined 300 patients with cardiovascular disease per month on an average; of these patients, 37 (12%) had nonvalvular AF (NVAF; 6.5% in India to 16.9% in Australia).

The survey revealed that NVAF patients were not always administered appropriate antithrombotic treatment. These data give us a foothold for the next step, i.e., the formulation, of the APHR Society practice guidelines.

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1. Background

Along with the aging of the population, the prevalence of atrial fibrillation (AF) has been rapidly increasing [1].
AF has been gaining much attention as one of the major causes of cerebral infarction [2], which highlights the importance of the establishment of antithrombotic treatment for AF patients. Thus far, guidelines for antithrombotic treatment have been published from Europe, the United States [3], Canada [4], and Japan (JPN) [5]. The European Society of Cardiology has recently published updated guidelines [6], including data on the verification of the effectiveness of direct thrombin and factor Xa inhibitors. However, no such guidelines have been established for the Asia-Pacific region, and optimal antithrombotic treatment for AF patients from this region has not yet been defined.

In 2010, the Asia-Pacific Heart Rhythm Society (APHRS) founded the “Practice Guideline Subcommittee” (Chairman: Satoshi Ogawa), with the main purpose of formulating its own guidelines. As part of the first step in its preparation, the subcommittee conducted a Web-based survey to understand the current practices in 9 Asia-Pacific countries for preventing stroke and systemic thromboembolism in non-valvular AF (NVAF) patients.

2. Methods

A Web-based survey was conducted among cardiologists in 9 Asia-Pacific countries. In 6 countries, the cardiologists on the registration lists prepared by the survey companies were sequentially asked to answer the questionnaire. Physicians meeting the following criteria were qualified to participate in the survey: those prescribing antithrombotic agents for NVAF patients, those who examined a minimum of 50 patients with cardiovascular diseases per month, those with clinical experience of 5–35 years, and those spending 50% of professional time in patient care. When 50 eligible responses were obtained, the survey was considered complete. In the remaining 3 countries (New Zealand, NZL; Singapore, SGP; and Hong Kong, HKG), there were no registration lists, and despite attempts by members of the subcommittee in each of these countries to seek the cooperation of the other members of the cardiovascular societies in their respective countries, less than 50 responses were obtained from these countries. The method of recruitment of subjects and the number of subjects varied among countries; therefore, the results are shown only for reference.

The number of beds in the medical facilities at which the physicians worked was variable, ranging from 9 beds or less in smaller clinics to 500 beds or more in hospitals. The results revealed that many physicians worked in small-scale facilities in India (IND). In China (CHN), Korea (KOR), Taiwan (TWN), and SGP, the majority of physicians worked in hospitals with 500 or more beds. This difference may have had some influence on the survey results.

The physicians surveyed the examined 300 patients with cardiovascular disease per month on an average, and of these, 37 (12%) had NVAF (Fig. 1). There were no significant differences among countries (5/76 patients or 6.5% in IND to 42/249 patients or 16.9% in Australia: AUS).

The percentage of NVAF patients treated with antithrombotic agents was 75% in the 9 countries on average; however, the percentage was the lowest (41%) in IND.

Physicians in these countries were asked questions pertaining to the following points:

1) Awareness and usage of guidelines (European Society of Cardiology [ESC], American Heart Association [AHA], American Collage of Cardiology [ACC], Japanese Circulation Society [JCS], and others).
2) Opinion on the need for an APHRS guideline.
3) Risk stratification of AF patients for prevention of thromboembolism.
4) Antithrombotic agents prescribed for prevention.
5) Satisfaction with current antithrombotic agents.
6) Expectations for new antithrombotic agents.
7) Others.

![Fig. 1. Physicians’ background: no. of patients.](image-url)
3. Results

3.1. Awareness and usage of guidelines

Among the guidelines of the ESC, AHA, ACC, JCS, and others, the ACCF/AHA/HRS 2011 guidelines [7] were the most frequently used in 4 countries, namely, AUS (56% of physicians), KOR (46% of physicians), TWN (52% of physicians), and SGP (65% of physicians). The ESC 2010 guidelines [6] were the most frequently used in 3 countries, namely, CHN (30% of physicians), HKG (44% of physicians), and NZL (59% of physicians). In JPN, 36% of the physicians used the JCS2008 [5], while in IND, 34% of the physicians used the ACC/AHA/ESC 2006 [3] and, interestingly enough, 10% used the JCS2008.

On an average, more than 77% physicians used guidelines published by the ACC, AHA, ESC, or HRS, while only 8% of those used the guidelines published from their own country.

3.2. Opinion on the need for an APHRS guideline

The physicians were asked to rate, on a 6-point scale, how strongly they felt the need for a guideline from the APHRS; the average score was 4.3, indicating that many physicians felt a strong need for a guideline from the APHRS (Fig. 2). In particular, in CHN, the average score was 5.0. On the other hand, the average score was 3.4 and 3.7 in NZL and AUS, respectively, indicating that the physicians in these countries were not as eager to have a special guidelines from the APHRS. This may be because approximately 60% of the physicians in these countries use, and are satisfied with, the ACC/AHA or ESC guidelines.

3.3. Reasons for desiring a guideline from the APHRS

The reasons for the physicians’ desire for a guideline from the APHRS were sought, and the following responses were obtained: (1) ethnic differences have not been taken into consideration in the existing guidelines (64%); (2) guidelines from the Western countries are not necessarily applicable to countries in the Asia-Pacific region (57%); (3) there are differences in the medical systems between Western and Asia-Pacific countries (43%); (4) available drugs are different in different regions (41%); and (5) underlying conditions of AF patients in Asia-Pacific countries are different from those in the United States and Europe (32%).

3.4. Antithrombotic agents prescribed for stroke prevention

With regard to the agents used for stroke prevention in NVAF patients, oral anticoagulants (OAC) were used in JPN; as much as 79% of the physicians in JPN used OACs, with 14% reporting concomitant use of antiplatelet agents (Fig. 3). This was also the case in AUS and SGP, where 78% of the physicians used OACs. On the other hand, half the physicians used antiplatelet agents alone in CHN, TWN, KOR, and IND, indicating that the superiority of OACs over antiplatelet agents had not yet been clearly established.

3.5. Antiplatelet agents prescribed for stroke prevention

Physicians using antiplatelet agents for stroke prevention were required to specify the type of the drugs used. A large majority of the physicians indicated that they used aspirin, with little difference among countries (Fig. 4).

3.6. Antithrombotic strategy according to CHADS2

Physicians were asked about the content of the antithrombotic treatment for patients with CHADS2 scores of 0, 1, and 2, i.e., patients with a history of stroke. It was found that for patients with a CHADS2 score of 0, most physicians use antiplatelet agents (63%) (Fig. 5). It was also found that the higher the CHADS2 score, the higher was the rate of warfarin use, and that a “no drug” policy was not employed for any patient with a CHADS2 score of 2 or higher. With respect to a CHADS2 score of 2, there were no significant differences in the content of therapy between patients with 2 risk factors and those with a history of stroke as the risk factor.

3.7. Antithrombotic strategy for patients with no risk factors (CHADS2 = 0)

In contrast, when we looked at individual countries, a large difference was observed (Fig. 6). According to the JCS2008, a CHADS2 score of 0 is indicative of a low-risk state and use of warfarin is not essential. Therefore, 46% of physicians in JPN employed the “no drug” policy for such patients. On the other hand, in other Asia-Pacific countries, the large majority of physicians characteristically used antiplatelet agents. The JCS2008 does not recommend the use of antiplatelet agents because of the increase in bleeding risk, which was reflected in the remarkably low rate of the use of antiplatelet agents (16%) in JPN. Further investigation is necessary to determine whether there are differences in the degree of recognition of the elevated risk of bleeding among countries and among ethnic groups.
3.8. Antithrombotic strategy for patients with 1 risk factor (CHADS2 = 1)

For patients with a CHADS2 score of 1, who are also judged to be low-risk patients, the treatment methods varied greatly among countries (Fig. 7). In IND, only 2% of the physicians used warfarin. On the other hand, in most of the other countries, the rate of warfarin use was as high as 40%. In JPN, 70% of the physicians used either warfarin or dabigatran, which was remarkably different from the case in the other countries. However, in the other countries, the usage rate of antiplatelet agents alone was also high for patients with CHADS2 = 1; particularly in IND, the usage rate of antiplatelet agents alone was as high as 70%.

3.9. Antithrombotic strategy for patients with CHADS2 score 2

For patients with a CHADS2 score of 2, the usage rate of OACs, including warfarin and dabigatran, was greater
than 70% in most countries (96% in AUS and SGP and 95% in HKG), whereas in IND again, 50% of these patients were treated with antiplatelet agents alone (Fig. 8).

3.10. Optimum international normalized ratio

Generally, the optimum international normalized ratio (INR) in all the countries was comparable to the recommended level by international guidelines, namely, an INR of 2 to 3 (Fig. 9). In IND, however, the lower limit was set at 1.4, a value that is almost ineffective, and the upper limit was set at 4.1, at which the risk of bleeding is markedly increased. In JPN, lower levels for the elderly were set at 1.6 to 2.6 according to the JCS2008, which was reflected in the results. A similar tendency was also observed in other countries, with the exception of IND.

3.11. Adjustment of the INR according to the age

The subjects were required to respond to the following question: “Do you alter the optimum INR setting depending on the age?” Half the physicians responded with “yes,” while the other half responded with “no” (Fig. 10). The average age at which they altered the optimum INR setting was 74 years. In IND, physicians altered the setting at 65 years, which is relatively low.
3.12. Antithrombotic treatment for paroxysmal AF vs. persistent AF

With regard to this topic, the subjects were asked the following question: “Do you prescribe antithrombotic treatment for paroxysmal AF in the same manner as that for persistent AF?” An average of 68% of the physicians, with a maximum of 91% in NZL, answered that they prescribed antithrombotic treatment for paroxysmal AF as well as for persistent AF (Fig. 11). On the other hand, this rate was low in TWN, IND, KOR, and CHN. These results indicate the lack of application of the recommendations of all current guidelines, which are in favor of using OACs for paroxysmal AF.

3.13. OAC during tooth extraction

Most physicians in JPN appeared to be aware of findings that tooth extraction can be safely performed while the patient is still taking warfarin. Surprisingly, however, in the other countries, the response from most of the physicians was “tooth extraction was performed after discontinuation of warfarin” (Fig. 12).

3.14. OAC during endoscopy or surgery

An overall average of 86% of physicians discontinued OAC administration during endoscopy or surgery, as per the guidelines; however, in IND, the majority of physicians
performed endoscopy and surgery without discontinuing OAC (Fig. 13).

3.15. OAC during cardioversion for persistent AF and paroxysmal AF

The overall average rate of warfarin use for cardioversion in cases of paroxysmal AF was lower than that in cases of persistent AF (59% vs. 73%), with a high positive response rate for antiplatelet agent use and “no drug” policy (Fig. 14). The rate of warfarin use was as low as 20% to 30% for both persistent and paroxysmal AF patients in IND.

3.16. Satisfaction rating for warfarin and antiplatelet agents on a 6-point scale

The results of the satisfaction rating for warfarin and antiplatelet agents on a 6-point scale are shown on the left and right sides, respectively (Fig. 15). With regard to

Q. Do you alter the optimum INR setting depending on the age?

![Figure 10. Adjustment of the INR according to the age.](47)
the satisfaction rating for warfarin, the highest score of 5.0 was observed for price, followed by the score of 4.6 for efficacy and evidence. The scores for bleeding risk, drug interaction, and diet restriction were around 3, clearly indicating that many physicians were dissatisfied with these factors. On the other hand, in the satisfaction rating for antiplatelet agents, the mean rating was 3.8, which was equivalent to that for warfarin; however, the score was 3.6 for efficacy, clearly lower than the corresponding score of 4.6 for warfarin.

### 3.17. Awareness level about new anticoagulants

Analysis of the responses to the question related to the degree of awareness about new anticoagulants in all 9 countries revealed that the awareness level was higher according to the degree of progression of the drug development around the world; 16, 22, 28, and 42% of the physicians indicated “I have never heard the name,” for dabigatran, rivaroxaban, apixaban, and edoxaban, respectively (Fig. 16).
3.18. Awareness about dabigatran

Dabigatran is already in the market in 6 countries, namely, AUS, JPN, TWN, HKG, NZL, and SGP and as expected, the awareness level about dabigatran was high in these countries (Fig. 17). However, it was somewhat surprising that as much as 12% of the physicians said “I have never heard the name,” in JPN, where dabigatran has been on the market since March 2011.

3.19. Top 3 reasons for prescribing dabigatran in place of warfarin

The reasons for prescribing dabigatran in place of warfarin were queried. Only the overall data for the 9 countries are shown in Fig. 18. Physicians prescribed dabigatran not because it can compensate for the disadvantages of warfarin, such as drug interaction and diet restriction, but because of the higher efficacy and lower
bleeding risk of dabigatran as compared with those of warfarin. This is evident from the data on the percentages assigned to the various reasons: efficacy, 77%; bleeding risk, 67%; and ease of administration, 55%. The prescription of dabigatran may have been based on the results of the RE-LY trial.

3.20. Awareness of CHA₂DS₂-VASC

The method of risk stratification for antithrombotic treatment was queried, and the results are shown in Fig. 19. About half the physicians in all countries used CHADS₂, and the other half used CHA₂DS₂-VASC. However, in NZL, 86% of the physicians used CHA₂DS₂-VASC, which was proposed by the ESC2010. This is probably because many physicians in NZL, as stated above, use the ESC guidelines. In JPN, however, 70% of the physicians used CHADS₂.

3.21. Awareness of the concept of Time in Therapeutic range (TTR)

Overall, 43% of the physicians answered they were aware of the concept of TTR, while 57% indicated that they were not (Fig. 20). The concept of TTR is important for stably
maintaining the preventive effect of warfarin, and awareness about this concept must be increased among physicians.

3.22. Awareness of the HASBLED (bleeding index)

HASBLED is defined as a risk factor for bleeding by the ESC2010, and more than half, that is, 57% of the physicians were aware of HASBLED (Fig. 21). Among 3 countries, namely, CHN, NZL, and HKG, where the ESC2010 appears to be the preferred guidelines, the awareness about HASBLED was low. The awareness levels were also low in JPN and KOR.

4. Discussion

Managing AF requires a comprehensive therapeutic strategy encompassing measures such as the prevention of complications from cerebral embolisms and heart failure, in addition to the treatment of the underlying disease and/or AF itself. Among these, the importance of anticoagulant therapy has been widely recognized. During the past 60 years, only a vitamin K antagonist, warfarin, was used to prevent cerebral and systemic thromboembolism for AF patients. However, regular monitoring of blood
coagulation was required to use warfarin safely and effectively. Thus, there has been a long wait for the development of much easier-to-use oral anticoagulants.

Under these circumstances, various oral anticoagulants are being developed, and a large-scale comparative trial with warfarin for AF patients is currently underway. The direct thrombin inhibitor, dabigatran, in particular, has attracted much attention because the RE-LY trial provided evidence that it lowers the risk of stroke/systemic embolisms without increasing the risk of hemorrhage, unlike warfarin [8,9]. Dabigatran has already been approved in the United States and Canada, as well as in 6 countries in the Asia-Pacific region. It is slated for approval in several other countries. The approval of new oral anticoagulants is expected to drastically change the antithrombotic treatment strategy for AF.

In the meantime, APHRS has launched activities to formulate regional-oriented guidelines by standardizing AF treatment in the Asia-Pacific region. This goal was set on the basis of the findings of a preliminary survey, which was conducted by the society’s Practice Guideline Subcommittee. The survey highlighted the difficulty in formulating comprehensive guidelines to cover the entire arrhythmia field in the region due to the huge differences among the nations with respect to the socio-economic status, medical-insurance systems, available drugs, and so on. Standardizing antithrombotic therapy for AF was chosen as the subcommittee’s first mission because the treatment methods for AF appear to be common throughout the region.

The scale of the survey was small, but it was the first trial of its type to cover the region. The status of the treatments unveiled in this survey was more or less as expected. The survey clarified the gaps among nations in a number of aspects, which reminds us of the need to standardize the treatments and at the same time of the difficulty in reaching the goal.

4.1. Background of surveyed countries’ physicians and dependence on guidelines

Although the number of patients for the physicians who participated varies among countries (from 76 in IND to 571 in TWN), on average, the physicians participating from the 9 countries examined 300 patients per month, and 37 patients (12%) of this group have NVAF. Since the ratio of patients with NVAF is not largely divergent among the countries, the figure can serve as the average ratio of patients with NVAF. With regard to whether physicians prescribe antithrombotic therapy to NVAF patients, 67–87% physicians in 8 countries answered in the affirmative. The exception was IND, with a figure of 41%. The APHRS member representing IND (NM) commented that doctors in India overestimate bleeding risk and underestimate stroke risk. While AF is managed, the need to prevent strokes is counterbalanced by the fact that warfarin therapy has its limitations. Reports from different laboratories on the INR have a high coefficient of variation. He (NM) added an example that the INR is reported to be 1.8, while the actual INR may be as high as 2.8. Then, doctors [in IND] tend to use lower doses of warfarin and accept lower INR ranges (below 2.0) as a result, and add aspirin and/or clopidogrel. Neither efficacy nor safety are addressed adequately in the process.

With regard to the awareness on usage guidelines for AF, only JPN uses its own guideline. Among the other countries, the United States and European guidelines are used extensively. At the same time, there are high expectations for guidelines specific to the Asia-Pacific area, especially in CHN. On the other hand, AUS and NZL show a lower level of interest. The APHRS member representing NZL (MS) was of the opinion that most cardiologists have received at least part of their training overseas, mainly in the United Kingdom or United States, and therefore, they may be comfortable following ACC/AHA or ESC guidelines.
4.2. Details of antithrombotic therapy

This study on the actual status of antithrombotic therapy surprisingly revealed that the use of antplatelet agents, including aspirin, was high in all the countries other than JPN (Fig. 3). Many clinical trials [10–12] have shown that aspirin is less efficacious than warfarin. The use of antplatelet agents was excluded from the JCS2008 guideline on the basis of the results of the Japan Atrial Fibrillation Stroke Trial (JAST) on lone AF [13], where the primary outcomes (3.1% per year) in the aspirin group were worse than those in the control group (2.4% per year) and treatment with aspirin caused a non-significant increase in the risk of major bleeding.

The APHRS member from NZL (MS) explains that probably, by prescribing aspirin, physicians at least feel they are doing something for stroke risk, and aspirin is seen as benign in terms of bleeding risk. There is considerable resistance to the use of warfarin due to the complexities in monitoring and dosing. Antplatelet therapy is a half-way step, which does not require monitoring and provides some stroke relief, especially for low-risk patients.

The CHADS2 score has been proposed as a tool for the stratification of risk from stroke in patients with AF [14]. Meta-analysis revealed that the net clinical benefit of warfarin would increase for patients with CHADS2 score of ≥ 2 [15], thereby justifying the recommendation of warfarin [3]. However, CHADS2 scores of 0–1, which account for over half of NVAF patients, have a risk of 1.9–2.8% per year for the development of strokes [14], as well as a risk for the development of left atrial thrombus [16]. These issues over the stratification of risks were highlighted for CHADS2 scores of 0 and 1 in the survey analysis of antithrombotic therapy (Fig. 5), i.e., 63% of physicians prescribed antplatelet agents at a CHADS2 score of 0 and 49%, at a CHADS2 score of 1. By country, JPN’s treatment strategy for low-risk factors showed a particularly interesting result. The JCS2008 guideline does not recommend warfarin for a CHADS2 score of 0. In addition, it excludes the use of aspirin as per the results of the JAST. Therefore, only 18% of physicians prescribed the antplatelet agent alone or as part of “combination therapy,” while 46% followed a “no drug” policy (Fig. 6). This trend was unique to JPN because most physicians in the other countries prescribed an antplatelet agent. This tendency was obvious at CHADS2 score of 1, wherein the ratio of the use of antplatelets in JPN was lower and that of the use of warfarin was higher than that in the other countries (Fig. 7).

The ESC2010 [6] guidelines recommend that anticoagulation treatment must definitively be administered for a CHADS2 score of ≥ 2, on the basis of the CHA2DS2-VASc score theory; the guidelines also stress that patients aged ≥ 75 years should be treated in the same manner as those with a score of ≥ 2. There is another stratification of risk at low-risk factors that are not included in the above conditions. According to the survey, the number of countries that use the CHADS2 and CHA2DS2-VASc scoring systems are almost the same. However, notably, in NZL, where the number of physicians who use the ESC2010 guidelines are high, 86% of physicians use CHA2DS2-VASC. In JPN, 70% of the physicians use CHADS2 (Fig. 19).

The rate of thromбоembolism risk is 1.67% and 0.78% per year for CHADS2 and CHA2DS2-VASc scores of 0, respectively, and 4.75% and 2.01%, for with scores of 1 [17]. This indicates that the CHA2DS2-VASc scoring system could identify relatively high-risk patients who need anticoagulation therapy among low-risk patients judged to be have a CHADS2 score of 0 or 1. In the ESC2010 guidelines, age 65–74 years, females, and vascular disease are categorized as “other risk factors” and for patients with 2 risk factors, antithrombotic therapy is recommended. Antithrombotic therapy or aspirin is recommended for patients with 1 risk factor, and no treatment (or aspirin) for patients with no risk factors. The fundamental difference between the JCS2008 and the ECS2010 is that the latter recommends aspirin for low-risk patients. It is necessary to clarify the net clinical benefit of prescribing aspirin for these patients.

The trends in JPN and NZL, where dabigatran is approved, indicate that the higher the risk, the higher the use of dabigatran, and particularly, in NZL, the rate of dabigatran use is higher than that of warfarin. These trends suggest that the relatively high rate of aspirin use may be related to the resistance to using warfarin (Fig. 8). Dabigatran has been approved in 6 Asia-Pacific countries to date, and antplatelet agents are expected to be gradually replaced by dabigatran in the future.

4.3. Actual status of warfarin usage

Warfarin is the only available oral anticoagulant agent, and studies based on meta-analysis have shown that it helps reduce the risk of strokes in NVAF by 68% [18]. However, when used, several conditions need to be followed. Despite its several limitations, warfarin was administered appropriately for patients with a CHADS2 score of ≥ 2, as recommended by the guidelines [3], in all countries except IND. The appropriate range of INR, in line with the international standard (2.0–3.0), was also observed in most countries. In order to prevent the risk of hemorrhages among the elderly, more than half the physicians in 7 countries answered that they modified INR in line with the patients’ age. Physicians in AUS and NZL answered “not modified,” but the maximum value indicated was less than 2.5 in both countries (Fig. 9).

With regard to the measures taken for patients on warfarin undergoing tooth extraction, endoscopy, or surgical procedures, the answers obtained from IND and JPN differed considerably from those obtained from the other countries. In JPN, 78% of the physicians recommended the continuation of anticoagulation therapy during tooth extraction, whereas most physicians in other countries stop the therapy. This is concerning because the patients are at a risk of embolism while the anticoagulation therapy is stopped. Serious thromboembolism occurs in about 1% of patients with AF after the discontinuation of warfarin [19,20]. Randomized controlled studies and observational studies have reported that tooth extraction can be safely performed on patients receiving antithrombotic drugs [21,22]. This was found as a common practice in JPN [5].
Until recently, dentists in JPN were also concerned about continuing warfarin administration for patients undergoing tooth extractions. However, the Japanese Association for Dental Science together with the Japanese Circulation Society have together provided sufficient evidence to eliminate this concern and have published relevant guidelines. Therefore, currently, tooth extractions in JPN are being conducted safely while continuing antithrombotic therapy.

### 4.4. Paroxysmal AF vs. Persistent AF

It seems to be well-accepted in most countries that paroxysmal AF and persistent AF pose the same risk of thromboembolism. In the 9 countries, an average of 68% of physicians answered that they administered antithrombotic therapy for both paroxysmal and persistent AF. On the other hand, the therapy during defibrillation varied, even among physicians who answered that there were the same risk factors with paroxysmal/persistent AF. The percentage of warfarin use was lower in the case of paroxysmal AF (59% versus 73%). However, in AUS, NZL, and SGP, 90–100% of the physicians prescribed anticoagulation therapy, including direct thrombin inhibitor for both paroxysmal and persistent AF, followed by JPN and HKG. On this point, IND again showed a large difference with respect to prescribing anticoagulation therapy; the percentages for paroxysmal and persistent AF were 38% and 36%, respectively.

In the other countries of CHN, KOR, IND, and TWN, 32–38% of physicians administered only antiplatelet agents during defibrillation for both paroxysmal and persistent AF. Although the evidence indicated that paroxysmal AF and persistent AF should be given equal importance [3,23], the survey revealed differences in the situation in the Asia-Pacific region. It is necessary to conduct a field survey on the rate of embolism during defibrillation.

### 4.5. Expectations for new developments in oral anticoagulant agents

Dabigatran can be administered in fixed doses, without the need for continuous monitoring. It also takes a shorter period than warfarin to confirm efficacy, and its disposition and pharmacodynamic action are predictable. There are no food restrictions during the intake of this drug, and cross-interaction with other agents is minimal. As indicated by the RE-LY trial [8,9], the use of dabigatran does not result in increases in the rates of major bleeding phenomena, while stroke and systemic embolism rates were lowered or remained unchanged. These points justify the positive promotion of dabigatran for AF therapy. According to the physicians participating in this survey, the characteristics of dabigatran, namely, efficacy, hemorrhage risk, and ease of dosage determination, render it a suitable replacement for warfarin. Further, awareness about factor Xa inhibitors, which are currently under development, was high, with physicians having big expectations for it.

### 4.6. Limitations of the study

The possibility that the results in each country were affected by the backgrounds of the physicians who participated in the Web survey is a major limitation of this study. When screening respondents to the questionnaire in this survey, physicians who (1) examined 50 or fewer patients with cardiovascular disease, (2) examined no patients with atrial fibrillation, or (3) had not administered antithrombotic therapy for NVAF patients during the last 1 month were excluded. However, even if these conditions were fulfilled, the experience and knowledge of the respondent physicians would have been uneven, because only 50 physicians were surveyed in each country. Therefore, the responses should be interpreted cautiously. For example, the number of beds in the hospitals in which the physicians worked was also uneven, and in IND, 44% of the physicians worked in small-scale hospitals with 9 beds or less. This may have caused the large differences in the view on antithrombotic therapy between physicians in IND and other countries.

Although the survey was rather small in scale and the results raised a number of concerns, it revealed that appropriate antithrombotic treatment was not always administered to NVAF patients in some countries. For the implementation of corrective measures, it will be necessary to determine the common features among and differences between the participating countries with respect to the different aspects of therapy. It is imperative to formulate an APHRS guideline for use in Asia-Pacific countries. We hope all the physicians who contribute to AF therapy in each country are made aware of the current situation through these survey results. We truly hope to gain momentum toward formulating guidelines.

### Conflict of interest

All authors have no conflicts of interest to declare.

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