Differences in Atrial Fibrillation Management Strategies among Physicians: A Survey Based Study

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Abstract

Aim: Previous data reflected confusions about classification and management of atrial fibrillation (AF) among physicians. Although relatively clear suggestions of dedicated guidelines, poor adaptation of them to routine clinical practice may result with suboptimal prevention and treatment measures. As a main stakeholder of management, physicians’ perceptions about the disease have major role. The study aimed to assess confusions and concordances of physicians about the definition and management of the disease. Methods and Results: We developed a web-based survey about AF consisting of 27 questions regarding valvular or non-valvular AF perception, using thromboembolic and bleeding risk scores, antithrombotic management and rate/rhythm control strategies. Two hundred and thirty two physicians participated and 224(97%) of them completed the survey. Although only cardiologists were invited to the survey, 27 physicians from different specialties also responded the survey. Half of the physicians reported that ≥40% of their patients had valvular AF. Dramatically, the survey responses revealed that nearly one-third of physicians classified the AF patients with mitral regurgitation as valvular AF. Most of the physicians denoted that they were using bleeding and stroke risk scores before deciding oral anticoagulation therapy and also preferring long term rhythm-control strategy in AF patients with systolic heart failure. However, results exposed evident disparities among physicians at specific aspects of the disease management. Conclusion: The survey-based study demonstrated a great heterogeneity in classification and management of AF among physicians because of guideline confusions/failures, inadequate evidence about some specific conditions and not being able to dominate the guidelines by physicians.

Keywords: Atrial fibrillation, management, physician, survey

INTRODUCTION

Atrial fibrillation (AF) is an independent risk factor for stroke and a significant predictor of mortality. Evidence-based AF guidelines recommend antithrombotic therapy corresponding to the risk of stroke.[¹] In practice, many patients with AF do not receive the appropriate antithrombotic therapy and are left either unprotected or inadequately protected against the risk of stroke.[²] Valvular AF has gained importance after the introduction of non-Vitamin K antagonists (NOACs) taking into account their contraindications.[³] The current guidelines have provided clear definition of the valvular AF.[⁴] Previous physician surveys showed heterogeneity in the perception of valvular AF.

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and variable thromboprophylactic strategies among physicians, particularly in the case of mitral regurgitation.\textsuperscript{[6,7]} Furthermore, recent European Heart Rhythm Association (EHRA) survey showed striking discordances in the definition and assessment strategies of valvular AF.\textsuperscript{[3]} The treatment threshold for the use of oral anticoagulants (OAC) differs between the current guidelines. Similarly, there is a controversy among the current guidelines regarding antithrombotic agent selection. Although according to the ACC/AHA/HRS guidelines aspirin (ASA) continues to have a role in the treatment of patients who have low stroke risk and cannot use OACs, the European Society of Cardiology (ESC) guidelines have entirely eliminated the use of ASA.\textsuperscript{[1,5]} These controversies in the guidelines may lead to significant differences in patient management in clinical practice.

NOACs have been emerged as an alternative to Vitamin K antagonists (VKAs) for thromboembolic prevention in AF patients. However, compared with VKAs, the proper use of NOACs requires many practical aspects. Practical guidelines about how to deal with NOACs in specific clinical situations have been published and updated by The European Heart Rhythm Association in recent years.\textsuperscript{[6,7]} Implementation of this guidance in clinical practice remained unclear.

The purpose of the survey was to obtain possible discrepancies on perception and management strategies of AF expressed by physicians in Turkey.

**The methodology of the survey**

We prospectively conducted a web-based survey for the opinions of physicians about AF. The study population was selected from a database composed of physicians who attended to the scientific activities of Society of Cardiovascular Academy. An electronic link of the questionnaire was sent to their E-mail addresses. The link deactivated after 6 months. The survey was voluntary, and no grant was given to the participants. Informed consent to participate in the survey and publication of the data was obtained by all involved physicians through Q26.

**Questionnaire development**

The questionnaire was developed by the second and last authors. Most of the questions were based on a multiple choice format. Due to the structure of the electronic questionnaire, skipping to the next question without giving an answer to the current question had not been allowed. The study was conducted according to the Declaration of Helsinki and its subsequent modifications. The demographic and personal data of each physician participated in the present survey were carefully preserved and strictly protected. The study was approved by the local ethics committee (Ege University, 26/01/2017-E.21845, 17-1.1.2).

**Survey questionnaire**

The survey questionnaire included a total of 26 questions addressing the following items: (1) Occupational demographics of physicians (Q01–Q05); (2) Perception of valvular AF (Q06–Q09); (3) Using stroke, bleeding risk scores and antithrombotic management strategies (Q10–Q12, Q16–Q17-Q20); (4) OAC therapy at specific scenarios (Q14–Q15, Q18, Q21–Q25); (5) Rhythm/Rate Control Strategies (Q13, Q19). The questionnaires were completed between January 2017 and July 2017.

**Data analysis**

Data were collected within the SurveyMonkey web site, exported to Excel (Microsoft, Redmond, WA) format, and imported into IBM SPSS (version 22.0 for Windows, Armonk, NY, USA) for statistical analysis. The answers to all questions were summarized as frequency counts and percentages. Because of the structure of the questionnaire, unanswered questions were not possible.

**Results**

The physician population included 197 cardiologists (88%), 10 cardiovascular surgeons (4.5%), 6 family physicians (2.7%), 5 internists (2.2%), 3 neurologists (1.3%), and 3 emergency physicians (1.3%). Of the 224 respondents, 125 (55.8%) had been in practice for >10 years, and 115 (51.3%) of them were working in education, research, and state hospital. Distribution of their academic degrees was as follows: 127 (56.7%)

### Table 1: Occupational demographics of physicians participating in the survey

| Question (n/text) | Answers, n (%) |
|------------------|----------------|
| Q1. What is your area of expertise? | Cardiology (197 (87.95)) |
| Cardiovascular surgery (10 (4.46)) |
| Internal diseases (5 (2.23)) |
| Neurology (3 (1.34)) |
| Emergency (3 (1.34)) |
| Family medicine (6 (2.68)) |
| Q2. How many years do you work as a physician? | <5 (20 (8.93)) |
| 5-10 (79 (35.27)) |
| >10 (125 (55.80)) |
| Q3. What is your academic status? | Trainer (17 (7.59)) |
| Specialist (127 (56.70)) |
| Assistant professor (23 (10.27)) |
| Associated professor (37 (16.52)) |
| Professor (20 (8.93)) |
| Q4. In which institution are you working? | Private hospital/medicine center (43 (19.19)) |
| Education Research Hospital, State Hospital (15 (6.74)) |
| University (61 (27.23)) |
| Family health center (5 (2.23)) |
| Q5. How often do you experience atrial fibrillation in 1 month? | 5%-10% (67 (29.91)) |
| 11%-20% (87 (38.84)) |
| 21%-30% (53 (23.66)) |
| 31%-40% (10 (4.46)) |
| >40% (7 (3.13)) |
specialists, 37 (16.5%) associated professors, 23 (10.3%) assistant professors, 20 (8.9%) professors, and 17 (7.6%) trainees. Occupational demographics of the population are detailed in Table 1.

Half of the physicians estimated that nonvalvular AF would account for ≥40% of all AF patients. A minority of the physicians (8.5%) thought that AF was valvular when associated with mitral regurgitation irrespective of its etiology and severity. Interestingly, 28% of physicians submitted that they decided valvular or nonvalvular AF according to the severity of mitral regurgitation [Figure 1]. While 74% of the physicians did not consider ischemic mitral insufficiency as valvular AF, 14% of them accepted ≥3° degree and more mitral insufficiency as valvular AF. Nearly 43% of the physicians thought that mitral insufficiency did not decrease the risk of thrombosis in the left atrium and appendix [Table 2].

Although 63% of physicians preferred to use OACs in AF patients who had CHA₂DS₂VASc score 1 for males (two for females), 21% of them specified ASA preference. Majority of physicians remarked CHA₂DS₂VASc score (97%) using for stroke risk classification and HAS-BLED score using (83%) for bleeding risk. The proportion of physicians using other bleeding risk scores was only 3%. While 26% of the physicians preferred ASA in older patients, more than half of the physicians did not prefer ASA in AF. Most of the physicians (71%) preferred to use CHA₂DS₂VASc ≥2 for the initiation of OACs in females with AF. According to almost half of the physicians, the daily doses of the NOACs (once or twice a day) were not important, but the other half of them did not agree [Table 3].

More than half of the physicians did not change doses of warfarin at the level of 1.9 INR in elderly patients. About 38% of physicians did not accept contraindications about OACs. About 48% of physicians did not prefer to use OACs therapies if the patient had any history of intracranial hemorrhage. In addition, 30% of the physicians did not consider giving OACs treatment in patients with a history of gastrointestinal bleeding. Nearly two-thirds of the physicians preferred to switch NOAC to warfarin if renal functions had decreased due to chronic diseases. In the case of the acute coronary syndrome, 75% of physicians pointed out clopidogrel preference in AF patients using OACs.

Only two physicians responded prasugrel preference [Figure 2]. More than half of the physicians considered switching warfarin to NOACs in AF patients who had low TTR levels, stroke/transient ischemic attack (TIA)/bleeding under warfarin and

**Table 2: Perception of nonvalvular atrial fibrillation by physicians**

| Question (n/text) | Answers, n (%) |
|-------------------|----------------|
| Q6. How many percentage of the cases you accept as NVAF? | 5-10 29 (12.95) 11-20 20 (8.93) 21-30 33 (14.73) 31-40 30 (13.39) >40 112 (50.00) |
| Q7. Can patients with unknown mitral valve diseases that have only mitral regurgitation (rheumatic and nonrheumatic) be classified as valvular atrial fibrillation? | Yes 19 (8.48) No 143 (63.84) Decision according to the degree of mitral insufficiency 62 (27.68) |
| Q8. What is the degree of mitral insufficiency for the diagnosis of valvular atrial fibrillation in patients with ischemic mitral insufficiency? | ≥1° 2 (0.89) ≥2° 16 (7.14) ≥3° 33 (14.73) Ischemic MR is NVAF 166 (74.11) No idea 7 (3.13) |
| Q9. Does mitral insufficiency decrease the thrombus formation in LA/LAA in patients with AF? | Yes 41 (18.30) No 97 (43.30) Only LA 41 (18.30) Both of them 30 (13.39) No idea 15 (6.70) |

NVAF: Nonvalvular AF, LA: Left atrium, LAA: Left atrial appendage
incompatibility. Furthermore, most of the physicians have thought to switch NOACs to warfarin in these conditions; drug side effects, stroke, and bleeding under NOACs. About 58% of the physicians preferred warfarin in AF patients with severe kidney diseases who had CHA\textsubscript{2}DS\textsubscript{2}VASc score of 3 and HASBLEED score of 2. The second preferred drug was apixaban 2.5 mg in severe kidney diseases by physicians (22%) [Figure 3]. Half of the physicians considered to start anticoagulation after the 1st day in AF patients with transient ischemic stroke [Figure 4 and Table 4].

Most of the physicians selected propafenone and amiodarone as the first-line agents for cardioversion (CV) in paroxysmal AF. Beta-blockers and digoxin were chosen by the majority of physicians (91% and 71%, respectively) as rate control
Table 4: Oral anticoagulant therapy at different scenarios

| Question (n/text)                                                                 | Answers, n (%)                  |
|----------------------------------------------------------------------------------|---------------------------------|
| Q14. What do you do if you detected 1, 9 INR levels in eighty or above ages patient under warfarin treatment? |                                 |
| I decrease                                                                      | 3 (1.34)                        |
| I increase                                                                      | 99 (44.20)                      |
| I do not change                                                                 | 122 (54.46)                     |
| Q15. Which of the following factors is reason for not giving OAC despite the indication of oral anticoagulant treatment? |                                 |
| Advanced age                                                                    | 21 (9.38)                       |
| Risk of patient failing                                                          | 26 (11.61)                      |
| Education level                                                                 | 41 (18.30)                      |
| Renal failure (stage 3 and above)                                                | 41 (18.30)                      |
| History intracranial hemorrhage                                                  | 107 (47.77)                     |
| Major GIS bleeding history                                                       | 67 (29.91)                      |
| None                                                                            | 86 (38.39)                      |
| Q18. What do you do if renal functions of NVAF patient under NOAC therapy show progressive deterioration due to underlying chronic diseases (HT, DM, Vascular disease, etc.,) (GFR<30 ml/min)? |                                 |
| Continue low dose of NOAC                                                       | 68 (30.36)                      |
| Change to warfarin                                                              | 145 (64.73)                     |
| Not medicate (OAC)                                                              | 11 (4.91)                       |
| Q20. Use single or double dose per day, do you influence your choice of NOAC?    |                                 |
| Yes                                                                             | 110 (49.11)                     |
| No                                                                              | 108 (48.21)                     |
| I have never used                                                               | 6 (2.68)                        |
| Q21. Which antiplatelet agent do you prefer with oral anticoagulant therapy after acute coronary syndromes in AF patients? |                                 |
| ASA                                                                             | 48 (21.43)                      |
| Klopidogrel                                                                     | 168 (75)                        |
| Tikagrelor                                                                      | 6 (2.68)                        |
| Prasugrel                                                                       | 2 (0.89)                        |
| Q22. Which cases do you switch warfarin to NOAC in NVAF patients? (Multiple options can be marked) |                                 |
| Directly                                                                        | 40 (17.68)                      |
| Low TTR levels (<65%)                                                           | 191 (85.27)                     |
| Stroke/TIA under warfarin therapy (although optimum INR levels)                  | 148 (66.07)                     |
| Hemorrhage under warfarin therapy                                                | 138 (61.61)                     |
| Patients does not want to follow INR levels                                      | 166 (74.11)                     |
| Limitation of logistics requirements                                            | 184 (82.14)                     |
| Never                                                                           | 2 (0.89)                        |
| Q23. Which situations do you switch NOAC therapy to other NOAC therapy or warfarin in NVAF patients? (multiple options can be marked) |                                 |
| Stroke/TIA associated therapy                                                    | 180 (80.36)                     |
| Hemorrhage associated therapy                                                    | 172 (76.79)                     |
| Side effect associated therapy                                                   | 203 (90.63)                     |
| No changing (focusing in trigger factors)                                       | 16 (7.14)                       |
| Q24. Which OAC do you prefer in AF patients that have 3 CHA2DS2-VASc score and 2 HAS-BLEED score if their creatinine clearance lowers 30 ml/min? |                                 |
| Warfarin                                                                        | 130 (58.04)                     |
| Dabigatran 110 mg                                                               | 23 (10.27)                      |
| Dabigatran 150 mg                                                               | 4 (1.79)                        |
| Rivaroxaban 5 mg                                                                | 5 (2.23)                        |
| Rivaroxaban 10 mg                                                               | 7 (3.13)                        |
| Apixaban 2, 5 mg                                                                | 49 (21.88)                      |
| Apixaban 5 mg                                                                   | 6 (2.68)                        |
| Q25. How many days after do you recommend oral anticoagulant therapy to AF patients with transient ischemic stroke? |                                 |
| 1 day                                                                           | 114 (50.89)                     |
| 2 days                                                                          | 11 (4.91)                       |
| 3-5 days                                                                        | 44 (19.64)                      |
| 1 week                                                                          | 36 (16.07)                      |
| 2 weeks                                                                         | 19 (8.48)                       |

INR: International normalized ratio, AF: Atrial fibrillation, NVAF: Nonvalvular AF, NOAC: Nonvitamin K antagonist oral anticoagulant, OAC: Oral anticoagulant, GIS: Gastro-intestinal system, GFR: Glomerular filtration rate, TIA: Transient ischemic attack
Table 5: Rhythm/rate control strategies

| Question (n/text)                                                                 | Answers, n (%) |
|----------------------------------------------------------------------------------|----------------|
| Q13. What is your first drug option in the pharmacological cardioversion of paroxysmal atrial fibrillation? |                |
| Beta blockers                                                                     | 31 (13.84)     |
| Propafenone                                                                       | 91 (40.63)     |
| Amiodarone                                                                        | 92 (41.07)     |
| Verapamil-diltiazem                                                               | 7 (3.13)       |
| Digoxin                                                                           | 3 (1.34)       |
| Q19. Which option do you prefer in AF patients that have ejection fraction below 40% for long-term heart rate control? (multiple options can be marked) |                |
| Digoxin                                                                           | 159 (70.98)    |
| Amiodarone                                                                        | 39 (17.41)     |
| Beta blockers                                                                      | 203 (90.63)    |

agents in AF patients with low ejection fraction [Table 5]. The last two questions (Q26, Q27) were about consent and address information.

**Discussion**

This survey has provided information about confusions and compatibilities of valvular and nonvalvular AF and usage of bleeding and risk scores in real life during the management of AF patients. In addition, the survey obtained physicians’ perspectives in terms of managing specific AF patient groups and in special situations.

The definition of valvular and nonvalvular AF has become more important after emerging of NOACs. Previous guidelines defined nonvalvular AF in the absence of a mechanical prosthetic heart valve or moderate to severe mitral stenosis (usually of rheumatic origin). The trials about NOACs have excluded mechanical prosthetic heart valve and mitral stenosis. In this study, half of the physicians accepted >40% of the patients were nonvalvular AF. These can be explained in three ways: (1) high prevalence of rheumatic valve diseases in our country due to the frequency of acute rheumatic fever, (2) nomenclature confusion of studies in literatures, and (3) physicians do not dominate the definitions in the current guidelines and are affected by the nomenclature confusions. More than half of the physicians in this survey evaluated mitral regurgitation as nonvalvular AF in patients with AF. Unlike this survey, in a previous study, most participants agreed that rheumatic mitral regurgitation was related to valvular AF. Perceptions of valvular AF are different among the studies because guidelines have different attitudes in valvular abnormalities other than prosthetic valves and mitral stenosis. Different designs of recent trials about NOACs led to confusions, gray zones in guidelines. While RELY trial excluded hemodynamically relevant valve diseases, ROCKET-AF study included patients who underwent annuloplasty, valvuloplasty, and commissurotomy. Furthermore, ARISTOTLE and ENGAGE trials did not include patients with moderate-to-severe mitral stenosis. Therefore, 2016 ESC guideline eliminated valvular AF to avoid confusion.

Some risk scoring methods were developed to evaluate the risk of stroke in the late 1990s in small cohort studies. The most commonly used and recommended score system by ESC guidelines is \( CHA_2 DS_2 VASc \) score. This scoring method firstly took place in ESC guidelines in 2010. In the light of the guidelines, almost all physicians (97%) preferred \( CHA_2 DS_2 VASc \) scoring method in AF patients. More than half of the physicians agreed to start OACs with \( CHA_2 DS_2 VASc \) score of 1 for males and 2 for females. In a previous study, most of the physicians (78%) thought that no additional research for starting anticoagulants when \( CHA_2 DS_2 VASc \) score ≥1 in AF patients. Some studies have shown that \( CHA_2 DS_2 VASc \) score of ≥1 for males and \( CHA_2 DS_2 VASc \) score of ≥2 for females was related with stroke and they would benefit from oral anticoagulant agents. OACs should be considered for patients after balancing the expected stroke risk, bleeding risk, and patient preference. In this survey, 70% of the physicians accepted the anticoagulant starting limit as \( CHA_2 DS_2 VASc \) of ≥2 for females, but current guidelines revealed that female gender alone does not appear to increase stroke risk in the absence of other stroke risk factors. There are some differences about the risk scoring system among guidelines. Unlike the American guidelines, European guidelines do not recommend antiplatelet agents in AF patients with a \( CHA_2 DS_2 VASc \) score of 0.

Most of the physicians (83%) preferred HAS-BLED bleeding risk score in AF as this score has been derived by using a real-world cohort of 3978 AF patients and it is a simple bleeding risk score system for physicians. Frequent use of bleeding risk scores by physicians in AF patients with high thromboembolic risk may be due to ensure the safety of patients. In a study, it was shown that 26% of AF patients with aged 80 years and over had stopped using OACs therapies for safety reasons in the 1st year. Especially, the intracranial hemorrhage risk related to fall is overestimated.

The physicians usually gave different responses about management of the patients with AF in specific scenarios. One of them was the management of elderly patients under subtherapeutic warfarin treatment. European guidelines depicted that OACs should not be avoided only due to age in elderly patients because of the higher risk of stroke in these people, but comorbidities should be taken into account. Although the most important contraindication of OAC therapies was intracranial hemorrhage in this survey, more than half of the physicians considered using OACs treatment after intracranial bleeding. Previous studies shown that less than half of the physicians have prescribed OAC therapies in geriatric syndromes, cognitive disorders and fall risk in elderly AF patients. Physicians are worried about prescribing OACs because of the high fall risk in elderly people. Furthermore, physicians feel responsible for intracranial hemorrhage after fall in the elderly patients using OACs. Hence, some physicians prefer ASA treatment in older AF patients for their safety and they consider that ASA is safer than warfarin and nearly as effective as it is. However, it has...
been revealed that AF patients with high thromboembolic risk would need to fall about three hundred times a year for the risk of intracranial hemorrhage.\[19\] The guidelines define that intracranial hemorrhage after anticoagulant interruption causes late ischemic strokes and death. Furthermore, guidelines point out that uncontrolled hypertension, aneurysm, triple antiagregan/anticoagulant therapy is not absolute contraindication, while only spontaneous intracranial hemorrhage is precisely contraindicated for anticoagulants.\[20\]

While approximately two-thirds of physicians preferred to switch NOAC to warfarin, one-third of them preferred to decrease NOACs’ doses in severe kidney failure diseases (glomerular filtration rate <30 ml/min/m²). There are not adequate data on the use of NOACs for stroke prevention in AF patients with severe chronic kidney disease because NOACs trials essentially excluded patients with CrCl of <30 ml/min/m² (except for a few patients on apixaban with CrCl of <30 ml/min/m²). Apixaban is approved by Food and Drug Administration in patients with creatinine clearance <15 ml/min or end-stage renal disease. However, the recommendations are based on pharmacokinetic and pharmacodynamic data of apixaban in severe kidney failure. In a meta-analysis of 43850 subjects, apixaban had a significantly lower bleeding rate than warfarin and thromboembolic event risks were similar in severe kidney diseases.\[21\] Today the European guidelines\[22\] suggest that apixaban, edoxaban, and rivaroxaban can be used in specific patients with CrCl of <30 ml/min/m². However, the lack of adequate trials and the difference of guidelines about renal disease may cause confusions and conflictions in physicians. Most of the physicians preferred clopidogrel as an antiplatelet agent in patients with AF who had acute coronary syndromes, 2016 ESC guideline and 2017 DAPT focused data recommends clopidogrel, ASA and NOACs as a triple therapy for acute coronary syndromes.\[1\] The NOACs are preferred because of their simple medication, causing less bleeding than warfarin in most cases and providing protection from stroke as warfarin.\[22\] For these reasons, the guidelines recommend the initiation of NOACs rather than warfarin, in patients with AF.\[1\]

There are no more randomized comparative trials of switching to NOACs versus VKA or NOACs treatment.\[23\] Switching NOAC-NOAC/NOAC-warfarin was found related to stroke and bleeding in the few previous studies. In a study, warfarin was preferred to NOACs because of previous VKA use, chronic renal failure, ischemic heart disease, and dabigatran use. The patients who preferred warfarin were young (<55) and had low CHA₂DS₂VASc score. Apixaban was tolerated by most patients using NOACs in this study. Hence, the patients who used other NOACs initially switched to apixaban during the study.\[24\] Users of apixaban had better persistence, this difference in persistence should be further explored. In this survey, physicians decided to switch drugs (NOAC-NOAC/NOAC-warfarin) because of stroke and bleeding under therapy (especially for secondary prevention), side effects and ease of use.

ESC guidelines\[23\] recommend that OACs may be continued (according to prescription and label) or started 1 day after a TIA after exclusion of intracranial bleeding by imaging modalities. However, half of the physicians in this survey preferred to start OACs 1 day after TIA. This shows that physicians are concerned about intracranial bleeding, they may not have enough information and they have confusions about this status. Physicians’ NOACs preferences were similar because there are no data in guidelines about NOACs preference.\[1\]

Most of the physicians preferred propafenone and amiodarone in paroxysmal AF as an antiarrhythmic agent and they chose beta blockers and digoxin for rate control in patients with low ejection fraction. European guideline\[1\] recommends flecainide and propafenone in patients without significant structural heart diseases and considers beta blockers and digoxin for long term rate control in LVEF <40% of patients. However, amiodarone could easily be found in our country which might be the reason for this preference. If there were more antiarrhythmic agents in our country, the physicians might have had confusions and differences about drug selections.

**Study limitations**

We did not group physicians according to their specialties and experiences. Perhaps we would have more homogenous responses if we had organized a survey with the same specialty and experience. And also we could not reach more physicians, so it was a limited study.

**Conclusion**

In this survey, the definitions of valvular and nonvalvular AF, specific patients’ managements were heterogeneous among physicians. This survey suggests that explorative data of NOACs phase III trials cannot convince most physicians and they have confusions and believe there is insufficient evidence about subgroup analyzes. Prospective multi-centered large randomized controlled trials focused on specific subgroups as kidney diseases, frail old patients, etc., and specific conditions are needed. Nowadays, the studies of NOACs with subgroups are underway and the results are expected in the world of medicine.

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**Conflicts of interest**

There are no conflicts of interest.

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