Epidemiology of atrial fibrillation in Turkey: preliminary results of the multicenter AFTER* study

Türkiye'de atriyum fibrilasyonu epidemiyolojisi; çok merkezli AFTER* çalışmasının ön sonuçları

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ABSTRACT

Objectives: Although atrial fibrillation (AF) is one of the most common rhythm disorders observed in clinical practice, a multicenter epidemiological study has not been conducted in our country. This study aimed to assess our clinical approach to AF based upon the records of the first multicenter prospective Atrial Fibrillation in Turkey: Epidemiologic Registry (AFTER) study.

Study design: Taking into consideration the distribution of the population in our country, 2242 consecutive patients with at least one AF attack determined by electrocardiographic examination in 17 different tertiary health care centers were included in the study. Inpatients and patients that were admitted to emergency departments were excluded from the study. Epidemiological data of the patients and the treatment administered were assessed.

Results: The mean age of the patients was determined as 66.8±12.3 years with female patients representing 60% of the study population. While the most common AF type in the Turkish population was non-valvular AF (78%), persistent/permanent AF was determined in 81% of all patients. Hypertension (%67) was the most common comorbidity in patients with AF. While a stroke or transient ischemic attack or history of systemic thromboembolism was detected in 15.3% of the patients, bleeding history was recorded in 11.2%. Also, 50% of the patients were on warfarin treatment and 53% were on aspirin treatment at the time of the study. The effective INR level was detected in 41.3% of the patients. The most frequent cause of not receiving anticoagulant therapy was physician neglect.

Conclusion: These results demonstrate the necessity for improved quality of physician care of patients with AF, especially with regards to antithrombotic therapy.

ÖZET

Amaç: Atriyum fibrilasyonu (AF) klinik pratiğimizde en sık rastlanan ritm bozukluğu olup ülkemizde bu konuda yapılmış çok merkezli bir epidemiyolojik çalışma bulunmamaktadır. Bu çalışmanın amacı ülkemizde ilk kez yapılmış olan çok merkezli, ileriye dönük Atrial Fibrillation in Turkey: Epidemiologic Registry (AFTER) çalışmasının kayıtlarından yararlanarak AF'ye klinik yönden yaklaşımımızı değerlendirmektir.

Çalışma planı: Ülkemizde nüfus dağılımı göz önünde bulundurularak 17 ayrı üçüncü basamak merkezden, elektrokardiyografisinde en az bir defa AF atağı tespit edilmiş olan ardışık 2242 hasta çalışmaya alındı. Acil polikliniğine başvuran ya da yatmakta olan hastalar çalışmadan dışlandı. Hastaların epidemiyolojik verileri ve uygulanan tedaviler değerlendirildi.

Bulgular: Çalışma popülasyonunu oluşturan hastaların %60'ı kadındı, hastaların ortalama yaşı 66.8±12.3 yıl olarak saptandı. Türk nüfusunda en sık görülen AF tipi non-valvular AF (%78) olup, AF'li hastaların %81'i ısrarcı-kalıcı AF'li idi. AF'ye en sık eşlik eden komorbid durum hipertansiyon (%67) olarak bulundu. Hastaların %15.3'ünde inme, geçici iskemik atak ve sistemik tromboemboli hikayesi mevcut iken kanama öyküsü hastaların %11.2'sinde kaydedildi. Çalışma süresinde hastaların %50'si warfarin, %53'ü de aspirin kullanıyordu. Oral antikoagülan ilaç kullanan hastaların %41.3'ünde etkin INR düzeyi saptandı. Oral antikoagülan ilaç kullanmamanın en sık nedeni (%69) hekim ihmali olarak saptandı.

Sonuç: Bu veriler klinik pratiğimizde özellikle AF'li hastaların antitrombotik tedavileri konusunda daha dikkatli olunması gerektiğini göstermektedir.

*AFTER: Atrial Fibrillation in Turkey: Epidemiologic Registry.

Atrial fibrillation (AF) is the most common rhythm disorder observed in our clinical practice.[1] Its prevalence in the general population is 1-2%.[2] As an important cause of cardiovascular mortality and morbidity with progressively increasing prevalence, AF has become a serious health issue at the present time. Most epidemiological studies suggest that AF will increase in frequency in the future. When the increasing and aging population in our country is considered, one can suggest that the presence of AF will be important to our society. However, studies conducted in our country do not indicate the actual characteristics of our society due to the single center nature of the studies, including their use of a limited number of patients[3-5] or the western origins of multicenter studies.[6-9] This study aimed to assess our clinical approach based on the first multicenter, prospective Atrial Fibrillation in Turkey: Epidemiologic Registry (AFTER) study of our country and the consistency with the guidelines.

PATIENTS AND METHODS

After taking into consideration the data provided by the Turkish Statistical Institute, 2242 patients were included in the study in a manner reflecting the population of the seven geographic regions.[10] A total of 17 tertiary health care centers agreed to participate in the study. These centers were interviewed and informed about the number of patients that they should admit according to the population of the city. The inclusion criteria were determined as "all consecutive patients over 18 years of age who applied to the cardiology outpatient clinics with at least one attack of AF identified on electrocardiographic examination". Emergency admittances, inpatients, patients who refused to be included in the study or had not signed the consent form were excluded from participating. Physical examination, weight and height measurements and electrocardiographic examination of each patient included in the study was performed.

The basic demographic data and medical treatments of the patients were evaluated. The evaluations of the patients were performed by a cardiologist and the data obtained were recorded in a patient registration form prepared for the study.

Types of AF were defined according to ESC guidelines.[2] Patient who present with AF for the first time are considered as first diagnosed AF, irrespective of the duration of the arrhythmia or the presence and severity of AF-related symptoms. Paroxysmal AF is defined as self-terminating, usually within 48 hours or 7 days. Persistent AF is considered as an AF episode that either lasts longer than 7 days or requires termination by cardioversion. Permanent AF is said to exist when the presence of the arrhythmia is accepted by the patient (and physician).

The stroke risk was assessed by CHA_2DS_2-VaSc score.[11] CHA_2DS_2-VASc depends on a point scoring system that gives 2 points for a stroke or transient ischemic attack and age ≥75 years and 1 point for each of the following factors: age between 65 and 74 years, history of hypertension, diabetes, recent cardiac failure, vascular disease (myocardial infarction, complex aortic plaque, prior revascularization, amputation due to peripheral artery disease or peripheral artery disease including angiographic findings) and female gender.[11] Hypertension was described as a blood pressure measurement >140/90 mmHg, prior diagnosis of hypertension or being on antihypertensive treatment. Diabetes mellitus was described as a fasting blood glucose level of >126 mg, prior diagnosis of diabetes or being on antidiabetic treatment. The routine total blood count parameters, International Normalized Ratio (INR) values, biochemical and thyroid function tests of the patients were performed in each center's own laboratory. Optimal INR was accepted as 2.0 to 3.0 as recommended by the guidelines.[2]

A consent form was signed by each patient. Ethics Committee consent of the study coordinating center was obtained.

Statistical analysis

SPSS 15.0 statistical package program ("Statistical Package for Social Sciences", Chicago, IL, USA) was used for data analysis. Continuous variables were expressed as mean ± standard deviation, categorical data were recorded as percentages.

RESULTS

The demographic characteristics of the patients included in this study are presented in Table 1. The mean age of the patients was 66.8±12.3 years (Fig. 1). While the most common AF type in the Turkish population was non-valvular AF (78%), permanent/persistent AF was present in 81% of all patients.

Table 1. Demographic characteristics of patients

	n	%	Mean±SD
Gender (Male / Female)	900 / 1342	40.1 / 59.9	
Age	2242		66.8±12.3
Age ≥75	669	29.8	
Body mass index	2227		27.8±5.3
Atrial fibrillation type			
Non-valvular	1745	77.8	
Valvular	497	22.2	
Prosthetic valve	280	12.5	
First attack	91	4.1	
Paroxysmal	328	14.6	
Persistent-permanent	1823	81.3	
Hypertension	1501	66.9	
Heart failure / LV dysfunction	641	28.6	
Type II diabetes mellitus	494	22	
Vascular disease	566	25.2	
Thyroid dysfunction	118	5.3	
Smoking	280	12.5	
Stroke / TIA / Thromboembolism	342	15.3	
Bleeding history	250	11.2	
Labile INR	252	11.2	
Effective INR	460	41.3	

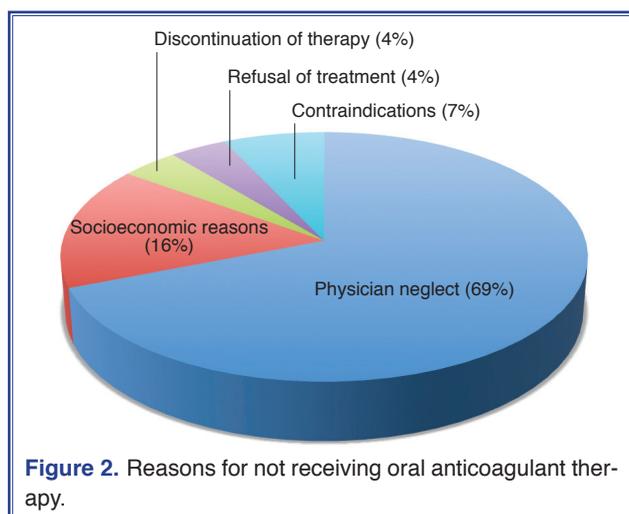LV: Left ventricle; TIA: Transient ischemic attack; INR: International normalized ratio.

Sixty percent of the patients with AF were female. Hypertension was the most common co-morbidity in patients with AF (67%). With regards to the other concomitant risk factors, 29% of patients had cardiac failure, 25% had vascular disease and 13% were smokers. A history of a stroke or transient ischemic attack or systemic thromboembolism was present in 15.3% of the patients and 11.2% of patients had a history of bleeding disorders.

Echocardiography was performed on the patients in this study and the average ejection fraction was 52.6±12.2% and the left atrial diameter was 4.7±0.8 cm. A spontaneous echo contrast in the left atrium or an image of a thrombus was observed in 5.8% of the patients.

41.3% of patients on oral anticoagulant therapy had an effective INR level. The INR value was labile in 11% of the patients. The results of basic laboratory tests of the patients are shown in Table 2.

The medications used by the patients are summarized in Table 3. 50% of the patients were on warfarin and 53% of the patients were on aspirin. The most
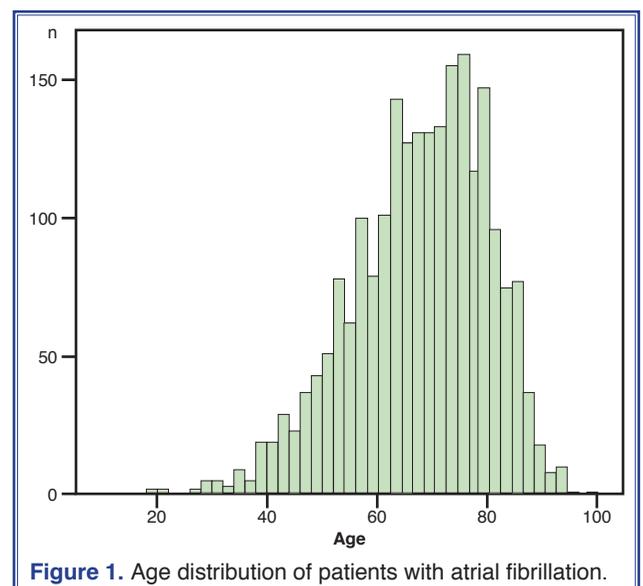
Figure 1. Age distribution of patients with atrial fibrillation.

Figure 2. Reasons for not receiving oral anticoagulant therapy.

The average age of all the patients with AF in our country was 66.8 years. The prevalence of AF in individuals over 75 years of age was 29%. These results were consistent with two large epidemiological studies (J-RHYTHM conducted in Japan and KORAF which studied Korean population) conducted with a methodology similar to that of the AFTER study.[6,7]

Table 2. Echocardiographic and biochemical variables of the patients

	n	%	Mean±SD
EF	2242		52.6±12.2
LA diameter	2242		4.7±0.8
LA SEC-thrombus	130	5.8	
Glucose	2226		119.9±46.3
Creatinine	2241		1.0±0.6
Total cholesterol	2228		177±43
Triglyceride	2228		136±80
HDL	2233		42±13
LDL	2233		111±34
INR	1115		2.43±1.54

EF: Ejection fraction; LA: Left atrium; SEC: Spontaneous echo contrast; HDL: High density lipoprotein; LDL: Low density lipoprotein; INR: International normalized ratio.

common medications used to treat comorbidities were beta blockers, diuretics and angiotensin converting enzyme (ACE) inhibitors.

For patients not on oral anticoagulant treatment, it was determined if the patient should actually be receiving oral anticoagulants according to the guidelines. The reasons for patients not receiving oral anticoagulants are summarized in Fig. 2. The most common and significant cause, present in 69% of cases, was the physician neglect. The rate of the discontinuation of the therapy by the patients without consulting their physicians was 4%, the rate of the refusal of the treatment was 4% and the rate of not receiving medication due to socioeconomic reasons such as not being able to have INR monitored, living alone or transportation problems was 16%. Only 7% of the patients were not receiving anticoagulant therapy due to a contraindication.

Table 3. Medications used by the patients

Medications	n	%
Warfarin	1115	49.7
Acetylsalicylic acid	1183	52.7
Clopidogrel	134	6
Ticlopidine	12	0.5
ACE-I	723	32.2
ARB	427	19.0
Beta-blockers	1316	58.7
Non-dihydropyridine CCB	355	15.8
Dihydropyridine CCB	171	7.6
Digoxin	622	27.7
Diuretics	1047	46.7
Statins	318	14.2
Alfa-blockers	40	1.8
Nitrates	65	2.9
Amiodarone	97	4.3
Propafenone	33	1.5

ACE-I: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; CCB: Calcium channel blocker.

DISCUSSION

The present study is the first multicenter AF study with a prospective design in our country. According to the preliminary cross-sectional data, 4/5 of AF cases in our country are non-valvular and can be classified as persistent/permanent. AF was 1.5 times more common in females than in males. The most common concomitant risk factor was hypertension. The prevalence of stroke was approximately 15%. When the whole cohort study was considered, approximately half of the patients were receiving oral anticoagulants and the major reason for not receiving oral anticoagulants despite oral coagulants being absolutely indicated was physician neglect.

In the AFNET study, which was conducted in Germany with 9582 patients, the average age was 68.4 years.[12] The higher average age in the western societies compared to the average age of AF in our country might be the explanation of this situation.

One of the interesting results of the AFTER study was that AF was found to be 1.5 times more common in females than in males. This result is consistent with the results of the TEKHARF study (Cardiac Diseases and Risk Factors in Adults in Turkey).[13] However, the incidence of AF was 1.5 to 2 times higher in females than in males according to the Framingham study performed in the United States of America.[14] While the Japanese society has a similar incidence in males compared to this study, the male-female rates were more similar to that of the Korean population.[6,7] Also, there was no difference in the prevalence of AF in the different geographical regions of our country. The predominance of valvular pathology-related AF in female patients in the subgroup analysis was 72% (358/497) and appears to contribute to the overall rate of female patients with AF (60%). This data shows that valvular heart disease still constitutes an important problem among the women of our country.

In our study, the prevalence of valvular pathology-related AF was 22%. This rate is among the highest of all developed countries. For example, the valvular pathology-related AF rate was found to be 14% in Japan and 9% in Germany.[6-12] It is very likely that the high prevalence of AF is related to the high frequency of rheumatic heart disease in our country. When the comorbidities accompanying AF were assessed, hypertension was the most common, which is consistent with other epidemiological studies performed on this subject.[6-12] The rate of coronary heart disease in our study was higher compared to the Japanese rate[6] and lower than the American rate.[9] While the concomitant cardiac failure rate in our cohort was found to be similar to the American, Spanish and German populations,[8,9,15] it was higher than the rate in the Japanese population.[6] According to a unicenter study, the American population has the highest rate of stroke at 20%.[9] In Germany, the stroke rate is 13%, which is similar to the AFTER study results. The relatively high rate of ischemic accidents in our population, despite the high rate of valvular AF, may be related to the older age of the patients in this study.

One of the most interesting results of our study was

that the INR levels were effective in less than half of the patients, even half of the patients were receiving oral anticoagulation therapy. The rate of patients who are on anticoagulation therapy was 67% in the Euro Heart Survey.[16] Another meta-analysis performed in America reported anticoagulation rates similar to the rate of our study.[17] However, the rate of patients who had an effective INR level was significantly worse in our study. In a meta-analysis of 50.000 patients, performed by van Walraven et al.[18] the INR was effective in 50% of the patients, compared to 41.3% of the patients in the AFTER study. The biggest reason for the lack of anticoagulation therapy, despite it being medically indicated, was the failure of physicians to start anticoagulation.

It was determined that the majority of the AF cases in our country were non-valvular and persistent/permanent, that the female patient population was larger than the male population, that the most common concomitant risk factor was hypertension, that the frequency of stroke was 15%, that the rate of anticoagulant use was 49% and the major cause for not receiving anticoagulation therapy was physician neglect. These results demonstrate the necessity for improved quality of physician care of patients with AF, especially with regards to anticoagulant therapy.

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REFERENCES

1. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, et al.. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001;285:2370-5.

2. European Heart Rhythm Association; European Association for Cardio-Thoracic Surgery, Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J 2010;31:2369-429.

3. Ertaş F, Duygu H, Acet H, Eren NK, Nazli C, Ergene AO. Oral anticoagulant use in patients with atrial fibrillation. Turk Kardiyol Dern Ars 2009;37:161-7.

4. Karaçağlar E, Atar I, Yetiş B, Corut H, Ersoy B, Yılmaz K, et al. The frequency of embolic risk factors and adequacy of anti-embolic treatment in patients with atrial fibrillation: a single tertiary center experience. Anadolu Kardiyol Derg 2012;12:384-90.

5. Ertaş F, Kaya H, Atılgan ZA, Elbey MA, Aydin M, Akil MA, et al. Predictors of warfarin use in patients with non-valvular atrial fibrillation who presented to the cardiology outpatient clinic of a tertiary hospital in Turkey: an observational study. Turk J Med Sci 2012;42:1172-9.

6. Atarashi H, Inoue H, Okumura K, Yamashita T, Kumagai N, Origasa H; J-RHYTHM Registry Investigators. Present status of anticoagulation treatment in Japanese patients with atrial fibrillation: a report from the J-RHYTHM Registry. Circ J 2011;75:1328-33.

7. Shin HW, Kim YN, Bae HJ, Lee HM, Cho HO, Cho YK, et al. Trends in Oral Anticoagulation Therapy Among Korean Patients With Atrial Fibrillation: The KORean Atrial Fibrillation Investigation. Korean Circ J 2012;42:113-7.

8. Schnabel RB, Wilde S, Wild PS, Munzel T, Blankenberg S. Atrial fibrillation: its prevalence and risk factor profile in the German general population. Dtsch Arztebl Int 2012;109:293-9.

9. Waldo AL, Becker RC, Tapson VF, Colgan KJ; NABOR Steering Committee. Hospitalized patients with atrial fibrillation and a high risk of stroke are not being provided with adequate anticoagulation. J Am Coll Cardiol 2005;46:1729-36.

10. Ertaş F, Kaya H, Yüksel M, Soydinç MS, Alan S, Ulgen MS. Atrial Fibrillation in Turkey: Epidemiologic Registry (AFTER) study design. Anadolu Kardiyol Derg 2013 Feb 6. [Epub ahead of print]

11. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 2010;137:263-72.

12. Nabauer M, Gerth A, Limbourg T, Schneider S, Oeff M, Kirchhof P, et al. The Registry of the German Competence NETwork on Atrial Fibrillation: patient characteristics and initial management. Europace 2009;11:423-34.

13. Uyarel H, Onat A, Yüksel H, Can G, Ordu S, Dursunoğlu D. Incidence, prevalence, and mortality estimates for chronic atrial fibrillation in Turkish adults. Turk Kardiyol Dern Ars 2008;36:214-22.

14. Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. Circulation 2004;110:1042-6.

15. Bover R, Pérez-Gómez F, Maluenda MP, Asenjo S, Pérez-Saldaña R, Igea A, et al. Long-term follow-up of atrial fibrillation patients in the NASPEAF study. Prospective evaluation of different antiplatelet treatments. Rev Esp Cardiol 2009;62:992-1000.

16. Nieuwlaat R, Capucci A, Camm AJ, Olsson SB, Andresen D, Davies DW, et al. Atrial fibrillation management: a prospective survey in ESC member countries: the Euro Heart Survey on Atrial Fibrillation. Eur Heart J 2005;26:2422-34.

17. Baczek VL, Chen WT, Kluger J, Coleman CI. Predictors of warfarin use in atrial fibrillation in the United States: a systematic review and meta-analysis. BMC Fam Pract 2012;13:5.

18. van Walraven C, Jennings A, Oake N, Fergusson D, Forster AJ. Effect of study setting on anticoagulation control: a systematic review and metaregression. Chest 2006;129:1155-66.