Atrial Fibrillation in Turkey: Epidemiologic Registry (AFTER) study design

Türkiye'de Atrial Fibrilasyon: Epidemiyolojik Kayıt (AFTER) çalışması dizaynı

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ABSTRACT

Objective: Atrial fibrillation (AF) is an important health problem in Turkey. However, no prospective, multicenter, large trial reflecting national data has been published so far. Therefore, the aim of this study was to follow, analyze and evaluate patients with AF in a large multicenter nation-wide trial.

Methods: Two thousand three hundred consecutive patients with AF in their electrocardiogram, reflecting all the population of seven geographical regions of Turkey will be included in the study. The patients will be followed up for two years and death, transient ischemic attack, stroke, systemic thromboembolism, major bleeding, hospitalization will be recorded as the primary end-point.

Results: Will be available at the end of the study; preliminary results will be due December 2012.

Conclusion: General risk profile of patients with AF, frequency of anticoagulation, frequency of effective treatment and risks of bleeding will be evaluated according to the current guidelines. Major adverse events and their independent predictors will be determined.

(Anadolu Kardiyol Derg 2013; 13: 339-43)

Key words: Atrial fibrillation, method, risk, prospective study

ÖZET

Amaç: Atriyal fibrilasyon (AF) ülkemiz için önemli bir sağlık sorunudur. Ülkemizde ileriye dönük, çok merkezli ve ülke epidemiyolojisini yansıtan ölçekte herhangi bir çalışma mevcut değildir. Bu çalışmayla ülkemizde çok merkezli bir çalışmada AF hastalarının epidemiyolojik verilerinin öne dönük olarak analizi, takibi ve değerlendirilmesi amaçlandı.

Yöntemler: Ülkemizden yedi coğrafi bölgeye ait nüfusu yansıtacak şekilde elektrokardiyografisinde en az bir defa AF atağı tespit edilmiş olan ardışık 2300 hasta çalışmaya alınacaktır. Hastalar ikinci yılın sonunda majör kardiyak sonlanım noktaları (ölüm, geçici iskemik atak, inme, sistemik tromboembolizm, major kanama ve hastane yatışı) açısından değerlendirilecektir.

Bulgular: Çalışma sonunda elde edilecektir. İlk bulguların Aralık 2012 tarihinde elde edilmesi planlanmaktadır.

Sonuç: AFTER (Atrial Fibrillation in Turkey: Epidemiologic Registry) çalışması ile kılavuzların önerileri doğrultusunda ülkemizdeki AF hastalarının genel risk profili, oral antikoagülan tedavi kullanım sıklığı, tedavi alan hastalarda hedef INR değerlerine ulaşılıp ulaşılmadığı ve hastaların kanama riskleri belirlenecektir. Çalışma sonunda ülkemizde AF'li hastalarda majör istenmeyen olay sıklığı ve bu olayların bağımsız belirteçleri de belirlenecektir. *(Anadolu Kardiyol Derg 2013; 13: 339-43)*

Anahtar kelimeler: Atriyal fibrilasyon, yöntem, risk, ileriye dönük çalışma

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia with a prevalence of 1 to 2% in the general population (1). AF leads to an increase in the risk of stroke by five times and one fifth of all strokes occur on a background of arrhythmia. The mortality, morbidity and recurrence rates of AF-related strokes are higher than other causes (2). According to the results of the TEKHARF (Cardiac Diseases and Risk Factors in Adults in Turkey) study, the prevalence of AF in our country is 1.25% and its overall

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morbidity is 6.8/100 person-year (3) It is obvious that AF is a significant health problem in our country. While there are many studies assessing the epidemiological data concerning the use of oral anticoagulant medication in patients with AF (4-8), single center studies on the anticoagulant therapy and the risk of cerebrovascular event have been conducted in our country (9-11).

However, no prospective, multicenter study on a scale reflecting the epidemiology of the country was conducted in our country.

In the multicenter Atrial Fibrillation in Turkey: Epidemiologic Registry (AFTER) study, we will prospectively examine the extent and epidemiological characteristics of the patients with AF.

Methods

Study design, sample size

AFTER study is planned as a prospective, observational and multicenter study and a 2-year follow-up of the patients.

In the anticipation of a total of 310 deaths and 650 events with a death rate of 6.8 and approximately 15 combined events per 100 person/year will be necessary for the multivariate logistic regression analysis intended to find out the independent indicators of the major adverse events. The follow up of 2300 patients for two years is calculated to be adequate. According to the data provided by the Turkish Statistical Institution, 2300 patients reflecting the population of the seven regions of our country will be included in the study.

Sample representation

First of all, all the tertiary centers from seven geographical areas were invited to participate. A sample representing the population of that geographical area was measured. After agreement, these centers were interviewed and informed about the number of the patients that they shall admit in the study according to the population of the area. The numbers of the patients included in the study according to the regions are shown in Figure 1. Overall, 17 tertiary health care centers agreed to participate in the study. The names and coordinators are shown in Table 1.

Algorithm of the trial

The main steps of the procedures are shown in Figure 2. The inclusion criteria will determine which patients are eligible for the participation to the study. The inclusion criteria are 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 refuse to be included in the study or do not sign the consent form will be excluded from the study. The standard registration form shown in Figure 3 will be filled out for each patient and the patients will sign a consent form.

Ethical considerations

Ethics Committee consent of the study coordinating center was obtained (The Ethics Committee of the University of Dicle; 28/3/2012-491). Every patient will sign a consent form.

Trial outcomes

Primary outcome considered is the major cardiac endpoints (death, transient ischemic attack, stroke, systemic thromboembolism, major hemorrhage and hospital admission). In addition, the medication condition of the patients will also be

Table 1. Coordinators and names of centers participating in AFTER study (by alphabetical order)

Faruk Ertaş, Hasan Kaya	Diyarbakır (Coordinator center)	Dicle University Faculty of Medicine
Alpay Arıbaş	Konya	Necmettin Erbakan University Meram Faculty of Medicine
Bayram Köroğlu	İstanbul	Siyami Ersek Education and Research Hospital
Bülent Vatan	Sakarya	Sakarya University Faculty of Medicine
Çağlar E. Çağlayan	Adana	Adana Numune Education and Research Hospital
Göksel Acar	İstanbul	Kartal Koşuyolu Education and Research Hospital
Mehmet Gül	İstanbul	Mehmet Akif Ersoy Education and Research Hospital
Mehmet Kanadaşı	Adana	Çukurova University Faculty of Medicine
Murat Yüksel	Malatya	Malatya State Hospital
Nihan Kâhya Eren	İzmir	İzmir Atatürk Education and Research Hospital
Nuri Köse	Muğla	Muğla Yücelen Hospital
Rüstem Yılmaz	Samsun	Samsun Gazi State Hospital
Selçuk Gedik	Ankara	Ankara Numune Education and Research Hospital
Serkan Bulur	Düzce	Düzce University Faculty of Medicine
Tolga Çimen	Ankara	Yıldırım Beyazıt University, Dışkapı Education and Research Hospital
Zekeriya Kaya	Şanlıurfa	Harran University Faculty of Medicine
Ziya Şimşek	Erzurum	Atatürk University Faculty of Medicine

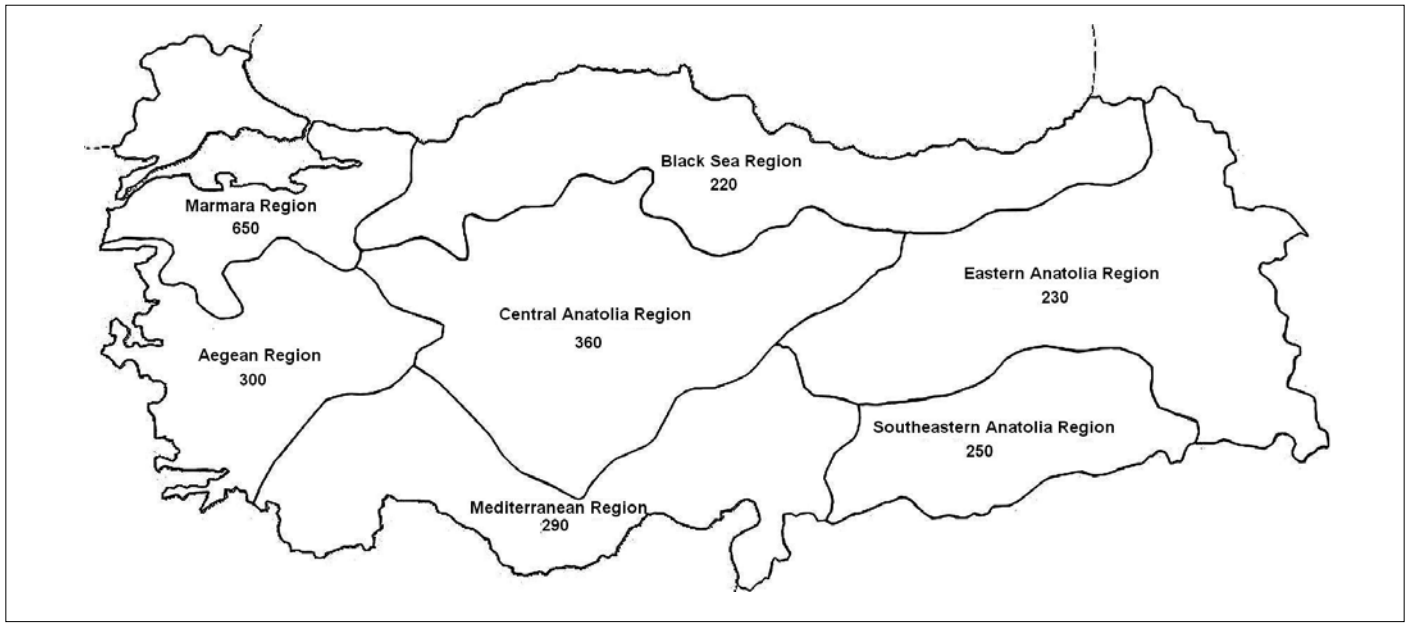


Figure 1. Regional distribution of patients in AFTER study

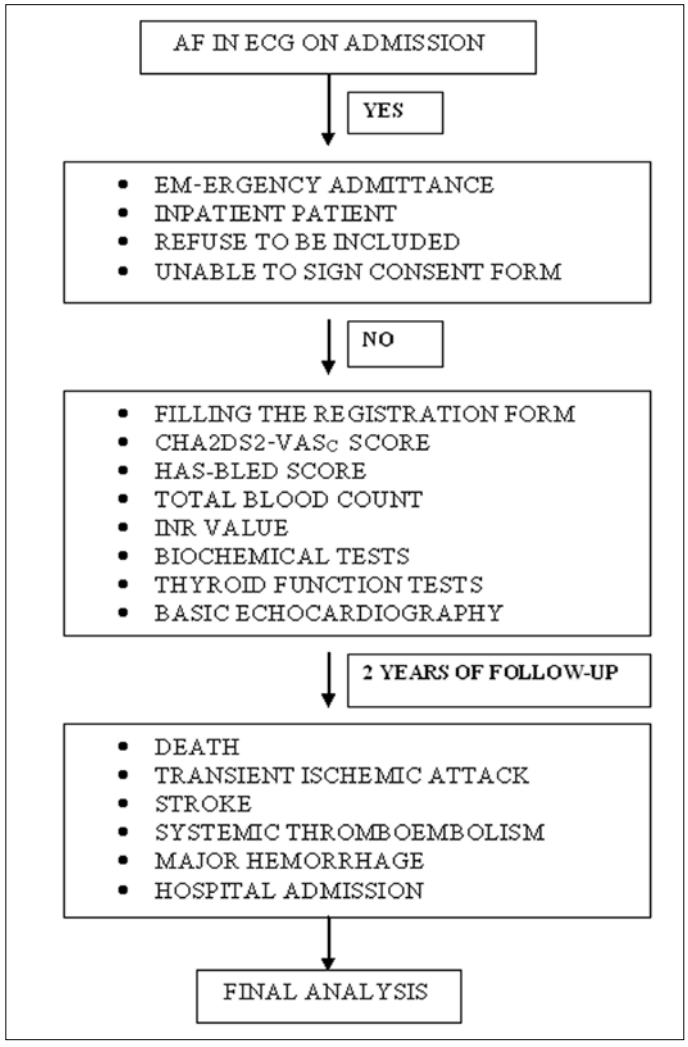


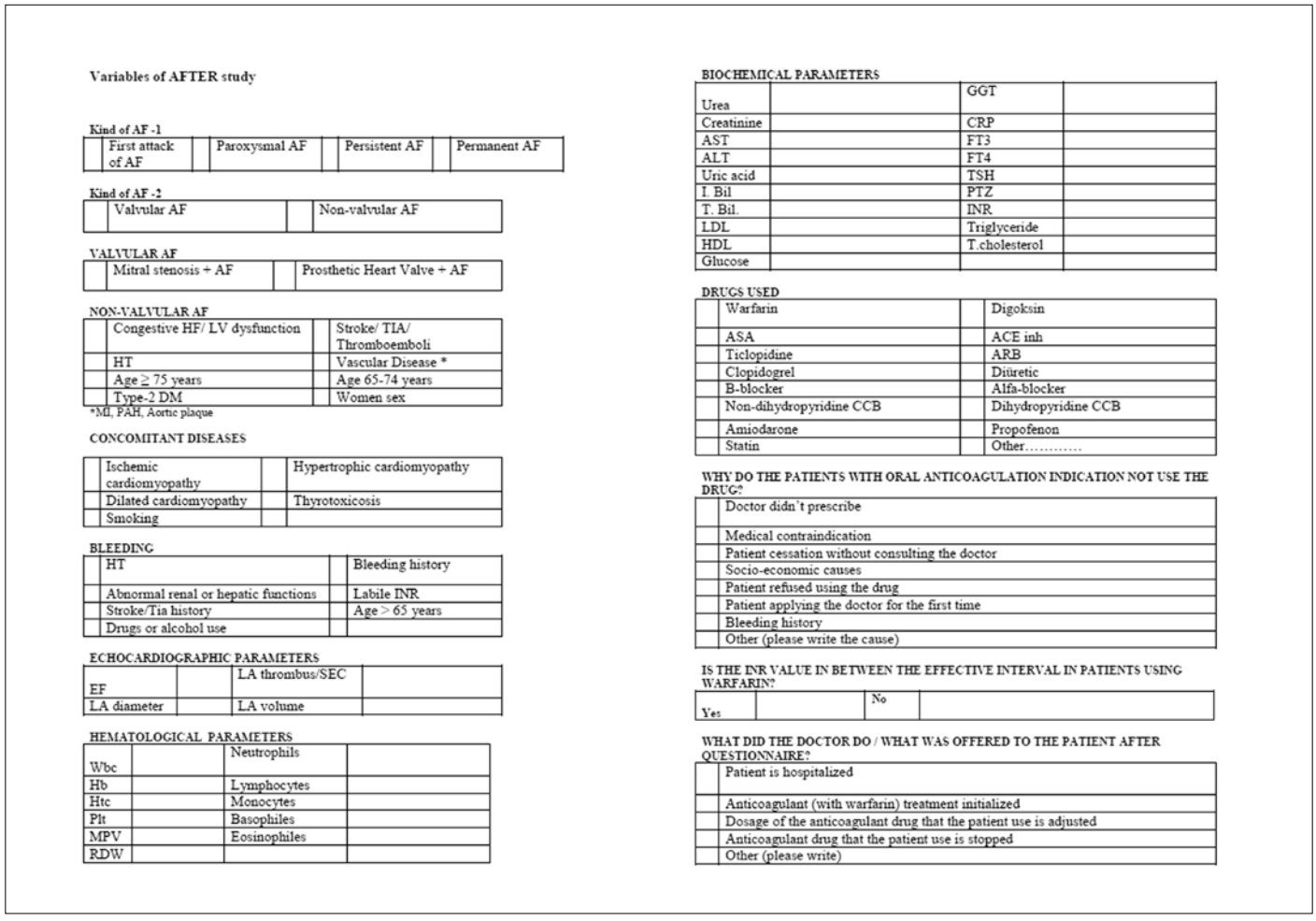
Figure 2. Main steps of the procedures
AF - atrial fibrillation

assessed. The inclusion of the patients in the study will be started in April 2012 and the date of the achievement of the targeted number of patients will be the ending date.

Definitions and measurements

The basic demographic data and medical treatments of the patients will be evaluated. The evaluation of the patient will be performed by a cardiologist and the data obtained will be recorded in a patient registration form prepared for the study. The stroke risk will be assessed by CHA2DS2-VASc score (12) and the bleeding risk will be assessed by the HAS-BLED score (13). CHA2DS2-VASc depends on a point scoring system that gives 2 points for 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 (12). Hypertension, abnormal renal/liver function, stroke, history of bleeding or tendency to bleeding, labile INR, advanced age (>65), concomitant drugs/alcohol are the parameters used in the calculation of HAS-BLED bleeding risk score (13). The routine electrocardiographic examination of the patients will be performed with regards to cardiac failure. Hypertension is described as 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, INR values, biochemical and thyroid function tests of the patients will be performed in each center's own laboratory. Optimal INR will be accepted as 2.0 to 3.0 as recommended by the guidelines (2).



Variables of AFTER study

Kind of AF -1

	First attack of AF		Paroxysmal AF		Persistent AF		Permanent AF

Kind of AF -2

	Valvular AF		Non-valvular AF

VALVULAR AF

	Mitral stenosis + AF		Prosthetic Heart Valve + AF

NON-VALVULAR AF

	Congestive HF/ LV dysfunction		Stroke/ TIA/ Thromboemboli
	HT		Vascular Disease *
	Age ≥ 75 years		Age 65-74 years
	Type-2 DM		Women sex

*MI, PAH, Aortic plaque

CONCOMITANT DISEASES

	Ischemic cardiomyopathy		Hypertrophic cardiomyopathy
	Dilated cardiomyopathy		Thyrotoxicosis
	Smoking		

BLEEDING

	HT		Bleeding history
	Abnormal renal or hepatic functions		Labile INR
	Stroke/Tia history		Age > 65 years
	Drugs or alcohol use		

ECHOCARDIOGRAPHIC PARAMETERS

EF		LA thrombus/SEC	
LA diameter		LA volume	

HEMATOLOGICAL PARAMETERS

Wbc		Neutrophils	
Hb		Lymphocytes	
Htc		Monocytes	
Plt		Basophiles	
MPV		Eosinophiles	
RDW			

BIOCHEMICAL PARAMETERS

Urea		GGT	
Creatinine		CRP	
AST		FT3	
ALT		FT4	
Uric acid		TSH	
I. Bil		PTZ	
T. Bil.		INR	
LDL		Triglyceride	
HDL		T.cholesterol	
Glucose			

DRUGS USED

	Warfarin		Digoksin
	ASA		ACE inh
	Ticlopidine		ARB
	Clopidogrel		Diüretic
	B-blocker		Alfa-blocker
	Non-dihydropyridine CCB		Dihydropyridine CCB
	Amiodarone		Propofenon
	Statin		Other……

WHY DO THE PATIENTS WITH ORAL ANTICOAGULATION INDICATION NOT USE THE DRUG?

	Doctor didn't prescribe
	Medical contraindication
	Patient cessation without consulting the doctor
	Socio-economic causes
	Patient refused using the drug
	Patient applying the doctor for the first time
	Bleeding history
	Other (please write the cause)

IS THE INR VALUE IN BETWEEN THE EFFECTIVE INTERVAL IN PATIENTS USING WARFARIN?

Yes		No	

WHAT DID THE DOCTOR DO / WHAT WAS OFFERED TO THE PATIENT AFTER QUESTIONNAIRE?

	Patient is hospitalized
	Anticoagulant (with warfarin) treatment initialized
	Dosage of the anticoagulant drug that the patient use is adjusted
	Anticoagulant drug that the patient use is stopped
	Other (please write)

Figure 3. Study registry form

Statistical analysis

Statistical Package for Social Sciences software (SPSS 12, Chicago, IL, USA) will be used for the data analysis. Normality analyses will be assessed using Kolmogorov-Smirnov and Shapiro-Wilks methods and data consistent with a normal distribution will be given as mean ± standard deviation and data inconsistent with a normal distribution will be given as median (minimum-maximum). In the comparison of quantitative data; normally distributed parameters will be compared between the two groups using the Student t-test and a one sided variance analysis (ANOVA) will be used in the comparison of more than two groups. The abnormally distributed parameters will be compared between two groups using Mann-Whitney U test and the Kruskal-Wallis test will be used in the comparison of more than two groups. The Chi-square test will be used for the comparison of qualitative data. Pearson test will be used in the correlation of the numeric variables and the Spearmen test will be used for the categorical variables. A multivariate logistic regression analysis will be used for the determination of the independent indicators of the primary endpoints, Kaplan's graphics and Cox hazard proportional analysis will be used for the survival analysis at the end of the study. A p value of <0.05 will be considered significant.

Discussion

Expected Benefit

In accordance with the recommendations of guidelines, the overall risk profile of the patients with AF in our country, the rates for the use of oral anticoagulant therapy and whether the targeted INR values are achieved or not and the bleeding risks of the patients will be determined in the AFTER study. At the end of the study, by detecting the prevalence of the major adverse events in patients with AF and the independent indicators of these events, the information directed to the clinical practice will be obtained, as well as a contribution will be provided to the literature.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - F.E.; Design - F.E., H.K., M.Y.; Supervision - F.E., H.K., M.Y.; Resource - F.E., H.K., M.Y.; Materials - F.E., H.K.; Data Collecting&Processing - AFTER araştırmaları; Analysis &/or interpretation - F.E.,M.S.S.; Literature search - M.S.A., M.S.Ü.; Writing - F.E., H.K. M.S.S., M.S.A.; Critical review - F.E., M.S.S., M.S.Ü.; Other -M.S.S., M.S.A., M.S.Ü.

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