

# Non-valvular atrial fibrillation in the elderly; preliminary results from the National AFTER (Atrial Fibrillation in Turkey: Epidemiologic Registry) Study

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**Abstract. – OBJECTIVE:** This study aimed at the assessment of the clinical approach to atrial fibrillation (AF) in the older population and the consistency with the guidelines based on the records of the multicenter, prospective AFTER (Atrial Fibrillation in Turkey: Epidemiologic Registry) study.

**PATIENTS AND METHODS:** 2242 consecutive patients admitted to the Cardiology Outpatient Clinics of 17 different tertiary Health Care Centers with at least one AF attack determined on electrocardiographic examination, were included in the study. Among the patients included in the study, 631 individuals aged 75 years and older were analyzed.

**RESULTS:** The mean age of the patients was determined as 80.3±4.2 years. The most frequent type of AF in geriatric population was the persistent-permanent type with a percentage of 88%. 60% of the patients with AF were female. Hypertension was the most common co-morbidity in patients with AF (76%). While in 16% of patients a history of stroke, transient ischemic attack or systemic thromboembolism was present, a history of bleeding was present in 14% of the patients. 37% of the patients were on warfarin treatment and 60% of the patients were on aspirin treatment. In 38% of the patients who were on oral anticoagulant treatment, INR level was in the effective range.

**CONCLUSIONS:** The rate of anticoagulant use in the elderly with AF was 37% and considering the reason of this situation was the medication not being prescribed by the physician, one should pay more attention particularly in the field of treatment.

*Key Words:*

Atrial fibrillation, Anticoagulation, Elderly, Predictor.

## Introduction

Atrial fibrillation (AF) as an important cause of cardiovascular mortality and morbidity, is an important health issue related to ischemic stroke and

other major complications affecting particularly the population aged over 75 years<sup>1,2</sup>. While AF prevalence is < 0% in 40-50 years, it gradually increases in a way that will be 5-15% by the age of 80<sup>3-7</sup>. As the age increases, AF-related stroke risk increases up to 23%<sup>8</sup>. In accordance with progressively increasing and ageing World population, AF prevalence and related adverse events increase. In our country the studies conducted on this subject have been unicenter and with a very limited number of patients<sup>9,10</sup>. Since the multicenter studies have been mostly conducted in western and far eastern populations, they do not reflect the characteristics of the country<sup>11-15</sup>. The aim of this study is the assessment of the clinical approach to AF in the older population and the consistency with the guidelines based on the records of a multicenter, prospective AFTER (Atrial Fibrillation in Turkey: Epidemiologic Registry) study.

## Patients and Methods

2242 consecutive patients admitted to the Cardiology Outpatient Clinics of 17 different tertiary Health Care Centers with at least one AF attack determined on electrocardiographic examination, were included in the study<sup>16</sup>. Among the patients included in the study, 631 individuals aged 75 years and older were assessed.

The inclusion criteria were determined as “all consecutive patients over 75 years of age who applied to the Cardiology Outpatient Clinics with at least one attack of AF identified on electrocardiographic examination and assessed by a cardiologist”. Patients with valvular AF, emergency admittances, inpatients, patients who had refused

to be included in the study or had not signed the consent form were excluded from the study. Detailed physical examinations, height-weight measurements and echocardiographic examinations of each patient included in the study, were performed. Besides, biochemical parameters and prothrombin time were measured. The patients were assessed according to 2010 ESC (European Society of Cardiology) guidelines in terms of the absolute anticoagulation criteria.

The Stroke Risk will be assessed according to CHA<sub>2</sub>DS<sub>2</sub>-VASc score<sup>17</sup> and the bleeding risk will be assessed according to the HAS-BLED score<sup>18</sup> CHA<sub>2</sub>DS<sub>2</sub>-VASc depends on a point scoring system that gives 2 points stroke and/or transient ischemic attack or age  $\geq 75$  years and 1 point for each of the following factors: age between 65 and 74 years, history of hypertension, diabetes mellitus, recent cardiac failure, vascular disease (myocardial infarction, complex atherosclerotic plaque, prior revascularization, amputation due to peripheral artery disease or peripheral artery disease (PAD) including angiographic results of PAD) and female gender<sup>17</sup>.

Hypertension, abnormal renal/liver function, stroke, history of bleeding or tendency to bleeding, labile INR, advanced age ( $> 65$ ), concomitant drugs/alcohol were the parameters used in the calculation of HAS-BLED<sup>18</sup>. A standard registration form was filled for every patient and a consent form was signed by the patients. Ethics Committee consent of the study coordinating center was obtained.

### Statistical Analysis

SPSS 12.0 statistical package program ("Statistical Package for Social Sciences" – SPSS Inc., Chicago, IL, USA) was used for data analysis. Continuous variables were expressed as mean  $\pm$  standard deviation, categorical data were given as percentages. A multivariate logistic regression analysis was used to assess the independent predictors of stroke. A  $p$ -value  $< 0.05$  was considered significant.

### Results

631 individuals aged 75 years and older included in the study were analyzed. The demographic characteristics of the patients are presented in Table I. The mean age of the patients was detected as  $80.3 \pm 4.2$  years. The most common type of AF in the geriatric population was the persistent-permanent AF. 60% of the patients with AF were female. Hypertension was the most common co-morbidity in patients with AF (76%). While a history of stroke, transient ischemic attack or systemic thromboembolism was detected in 16% of all patients, a history of bleeding was detected in 14% of the patients. INR was in the affective range in 38% of the patients who were on oral anticoagulation medication. Labile INR was observed approximately in one out of the every ten patients.

The basic biochemical and echocardiographic variables of the patients are shown in Table II. In the echocardiographic examinations of the pa-

**Table I.** Demographic characteristics of the patients.

Demographic characteristics		n	%	Mean $\pm$ SD
Sex	Male	251	39.8	
	Female	380	60.2	
Age				80.3 $\pm$ 4.2
BMI				26.5 $\pm$ 4.9
	First attack	16	2.5	
	Paroxysmal	60	9.5	
	Persistent-permanent	555	88	
Hypertension		482	76.4	
Heart failure-LV dysfunction		219	34.7	
Type 2 diabetes mellitus		133	21.1	
Vascular disease		226	33.8	
Thyroid dysfunction		43	6.8	
Smoking		52	8.2	
Stroke-TIA-thromboembolism		99	15.7	
History of bleeding		88	13.9	
Labile INR		66	10.5	
Effective INR		87	37.7	

BMI: body mass index LV: left ventricle TIA: transient ischemic attack INR: international normalized ratio.

**Table II.** Echocardiographic and biochemical variables of the patients.

	%	Mean $\pm$ SD
EF		51.5 $\pm$ 12.2
LA diameter		4.7 $\pm$ 0.6
LA SEC-thrombus; n = 36	5.7	
Glucose		117 $\pm$ 38
Creatinine		1.1 $\pm$ 0.6
Total cholesterol		170 $\pm$ 42
Triglycerides		121 $\pm$ 66
HDL		42 $\pm$ 13
LDL		106 $\pm$ 34
INR; n = 231		2.4 $\pm$ 1.5

EF: ejection fraction. LA: left atrium. SEC: spontaneous echo contrast. HDL: high density lipoprotein. LDL: low density lipoprotein INR: international normalized ratio.

tients the mean ejection fraction was detected as 51.5 $\pm$ 12.2% and the left atrium diameter was detected as 4.7 $\pm$ 0.6 cm. Spontaneous echo contrast in the left atrium or thrombus image were observed in 6% of the patients.

37% of the patients were on warfarin treatment and 60% of the patients were on aspirin treatment. Most common medications used for the comorbidities were beta blockers, diuretics ACE inhibitors and digoxin. The most common reason of not receiving anticoagulant medication in spite of the presence of an absolute indication according to the guidelines, was the physician neglect with a percentage of 66%.

The rate of the therapy discontinued by the patients without consulting their physicians was 3%, the rate of the refusal of the treatment was 4% and the rate of not receiving medication due to socioeconomic reasons was found as 18%. In 8% of the patients, there was a contraindication for anticoagulation.

Multivariate logistic regression analysis was used to identify independent determinants of stroke (Table III). The covariates considered were CHA<sub>2</sub>DS<sub>2</sub>-VASc score, HASBLED score

and effective warfarin use. CHA<sub>2</sub>DS<sub>2</sub>-VASc and HASBLED scores were found to be the independent predictors of stroke in the elderly (odds ratio: 4.69 [95% confidence interval: 3.47-6.33];  $p < 0.001$  and OR = 1.46 [95% CI 1.10-1.93];  $p = 0.009$ ; respectively).

## Discussion

The present study is a multicenter study with prospective design conducted in the population with non valvular AF, aged 75 years and older. According to the analysis of the preliminary records, almost all of the AF cases were included in the persistent/permanent group. The other remarkable results were the dominance of females at a rate of 1.5 fold, the determination of hypertension as the most common concomitant risk factor and a stroke prevalence of 16%. When the whole cohort study was considered, while only 1/3 of the patients were receiving oral anticoagulants, the major reason of not receiving oral anticoagulant in spite of an absolute indication was determined as physician neglect.

In this work the mean age of the patients with non valvular AF aged 75 years and older, was found as 80 years. This result is consistent with the results of BAFTA study<sup>19</sup>. One of the interesting results of AFTER study was that the frequency of female patients was 1.5 times higher than the frequency of male patients with non-valvular AF aged 75 years and older. This result is consistent with the findings of the study compiled by Feinberg et al<sup>20</sup>. However, according to records of BAFTA study which studied English population, the frequency of AF was higher in males than in females (54%). Japanese records also had a similar male patient frequency<sup>19</sup>.

When comorbidities in patients with AF were assessed, similarly to the results of many epidemiological studies on this subject, hypertension was observed as the most common comorbidity<sup>19,22,23</sup>. While in Spanish society, coronary artery

**Table III.** Logistic regression analysis of the independent predictors of stroke/TIA/thromboembolic events.

	Odds rate	95% confidence interval	p value
CHA <sub>2</sub> DS <sub>2</sub> VaSc score,	4.69	3.46-6.33	< 0.001
HASBLED score	1.46	1.10-1.93	0.009
Effective INR	0.86	0.41-1.79	0.860

TIA: transient ischemic attack; INR: international normalized ratio.

disease was less frequent than Turkish society<sup>22</sup>, coronary artery disease was more frequent in the American population<sup>12</sup>. While the rate of concomitant heart failure was observed to be similar to those of American and German populations in AFTER cohort. It was less than English and Spanish populations<sup>19,22</sup>. When the populations were compared in terms of the history of stroke, the highest rate with a percentage of 19%, was observed in a unicenter study conducted in the German population<sup>23</sup>, in Spanish population a rate of 16% was found similar to the results of AFTER, and in the English population, lower rates with a percentage of 13% were determined<sup>19</sup>.

37% of the patients were on warfarin treatment and 60% of the patients were on aspirin treatment. One of the most interesting results of our study was that the effective INR levels were provided only in 38% of the patients. Although the anticoagulant use rate was consistent with the literature<sup>23</sup>, the effective INR levels were significantly worse in our country. In the meta-analysis of 50 thousand patients, performed by Walraven et al<sup>24</sup> the rate of staying in the effective range was reported as 50%. This rate was found as 41.3% in the AFTER study. While, not starting the anticoagulation therapy by the physician was in the first rank with a percentage of 66% among the causes of not receiving oral anticoagulation therapy in spite of the absolute indication, it brings a great responsibility to our physicians. The determination of CHA<sub>2</sub>DS<sub>2</sub>-VASc and HASBLED scores as independent stroke predictors in our study might be related to the presence of the common comorbidity factors between the two scoring systems such as age, hypertension, history of stroke. However the presence of the relationship between HASBLED score and history of stroke independently from CHA<sub>2</sub>DS<sub>2</sub>-VASc, suggests the necessity of preferring the new agents<sup>25-27</sup> that provide better protection with lower risk of bleeding, in this group of age with the higher risk of stroke and lower rate of warfarin use due to the monitoring difficulties.

## Conclusions

It was observed that the majority of the AF cases were included in persistent/permanent group, the female sex was dominant over the male population, the most common concomitant risk factor was hypertension. The rate of anticoagulant use was 37% and the reason of this situation was the

medication not being prescribed by the physician. These results showed that in our practices with elderly patients with AF, more attention should be paid, particularly in the field of treatment.

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## Conflict of Interest

We certify that there is no any conflict of interest with any financial organization regarding the material discussed in the manuscript.

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