Turk Kardiyol Dern Ars 2018;46(2):92-102 doi: 10.5543/tkda.2017.79367

ORIGINAL ARTICLE

Clinical practices of the management of nonvalvular atrial fibrillation and outcome of treatment: A representative prospective survey in tertiary healthcare centers across Turkey

Non-valvüler atriyum fibrilasyonu yönetiminde klinik uygulamalar ve tedavi sonuçları: Türkiye genelindeki üçüncü basamak sağlık merkezlerinde yapılan ileriye dönük anket çalışması

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ABSTRACT

Objective: The goal of this study was to define clinical practice patterns for assessing stroke and bleeding risks and thromboprophylaxis in nonvalvular atrial fibrillation (NVAF) and to evaluate treatment outcomes and patient quality of life.

Methods: A clinical surveillance study was conducted in 10 tertiary healthcare centers across Turkey. Therapeutic approaches and persistence with initial treatment were recorded at baseline, the 6th month, and the 12th month in NVAF patients.

Results: Of 210 patients (57.1% male; mean age: 64.86±12.87 years), follow-up data were collected for 146 patients through phone interviews at the 6th month and 140 patients at the 12th month. At baseline, most patients had high $CHADS_2$ score (≥2: 48.3%) and CHA_2DS_2-VASc (≥2: 78.7%) risk scores but a low HAS-BLED (0–2: 83.1%) score. Approximately two-thirds of the patients surveyed were using oral anticoagulants as an antithrombotic and one-third were using antiplatelet agents. The rate of persistence with initial treatment was approximately 86%. Bleeding was reported by 22.6% and 25.0% of patients at the 6th and 12th month, respectively. The proportion of patients with an INR of 2.0–3.0 was 41.8% at baseline, 65.7% at the 6th month, and 65.9% at the 12th month. The time in therapeutic range was 61.0% during 1 year of follow-up. The median EuroQol 5-dimensional health questionnaire (EQ-5D) score of the patients at baseline and the 12th month was 0.827 and 0.778, respectively ($p<0.001$). The results indicated that patient quality of life declined over time.

Conclusion: In atrial fibrillation, despite a high rate of persistence with initial treatment, the outcomes of stroke prevention and patient quality of life are not at the desired level. National health policies should be developed and implemented to better integrate international guidelines for the management of NVAF into clinical practice.

ÖZET

Amaç: Non-valvüler atriyum fibrilasyonunda (NVAF), hastaların felç ve kanama riski ve tromboprofilaksi açısından değerlendirilmesi için klinik uygulama paternlerini belirlemek ve hastaların tedavi sonuçlarını ve yaşam kalitelerini değerlendirmek.

Yöntemler: Türkiye genelinde 12 üçüncü basamak sağlık merkezinde yürütülen klinik sürveyans çalışma. Tedaviye yaklaşım ve tedaviye uyum verileri NVAF'li hastalarda çalışma başlangıcında, 6. ve 12. aylarda kaydedildi.

Bulgular: Takip verileri, 210 hastanın (%57.1 erkek; ortalama yaş, 64.86±12.87 yıl) 146'sında 6. ayda ve 140'ında 12. ayda telefon görüşmesiyle toplandı. Başlangıçta, hastaların çoğunda $CHADS_2$ (≥2, %48.3) ve CHA_2DS_2-VASc (≥2, %78.7) risk skoru yüksekken HAS-BLED (0-2, %83.1) skoru düşüktü. Başlangıçta, 177 hasta (%84.3) herhangi bir AF tedavisi alıyordu. Antitrombotik tipini bildirenlerin yaklaşık üçte ikisi oral antikoagülan ve üçte biri antitrombosit ajan kullanıyordu. Başlangıç tedavisine devam oranı yaklaşık %86'ydı. Kanama 6. ayda hastaların %22.6'sında ve 12. ayda %25'inde bildirildi. Hedef INR değeri 2–3 olan hastaların yüzdesi başlangıçta %41.8 iken, 6. ayda %65.7'ye ve 12. ayda %65.9'a yükseldi. Bir yıllık takipte, terapötik aralıkta geçen zamana hastaların %61.0'ında ulaşıldı. Hastaların medyan EQ-5D skorları başlangıçta 0.827 (0.145–1.000) ve 12. ayda 0.778 (-0.040–1.000) idi ($p<0.001$). Sonuçlar, hasta yaşam kalitesinin zamanla azaldığını gösterdi.

Sonuç: Atriyum fibrilasyonunda, tedavi ve başlangıç tedavisine devam oranlarının yüksekliğine rağmen tromboprofilaksi sonuçları ve hastaların yaşam kaliteleri istenen düzeyde değildi. Ulusal düzeyde sağlık politikaları geliştirilmelidir. NVAF'nin uluslararası kılavuzunu klinik uygulamaya daha iyi entegre etmek için ulusal sağlık politikaları geliştirilmeli ve uygulanmalıdır.

Received: October 14, 2016 *Accepted:* November 16, 2017

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Atrial fibrillation (AF) is the most common sustained arrhythmia, affecting 1% to 2% of the population.[1–3] The prevalence of AF increases with age, reaching 15% at 80 years.[3] Being a significant independent thromboembolic risk factor, AF causes a 5-fold increase in the risk for stroke, and 1 in 5 of all strokes are attributed to AF.[4] Ischemic strokes associated with AF are often fatal, and those patients who survive are frequently disabled and more likely to have a recurrence compared with patients with other causes of stroke.[5]

The appropriate thromboprophylaxis is central to the management of AF for the prevention of stroke. These treatment targets should be monitored closely from the first presentation, particularly in patients with newly diagnosed AF.

Treatment options in patients with AF should be individualized based on the risk (bleeding) versus benefit (prevention of stroke) of therapy, which is often difficult to assess.[6] Recent clinical guidelines suggest using several scoring tools, such as $CHADS_2$ (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism) and CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, female) to evaluate the risk of stroke, or HAS-BLED (hypertension, abnormal renal or hepatic function, stroke, bleeding, labile international normalized ratio [INR], age ≥65 years, drugs or alcohol) to evaluate the risk of bleeding.[4,6–8]

Thus, in the present study, the primary aim was to define the practice patterns for the assessment of stroke and bleeding risk and treatment to prevent thromboembolism in patients with nonvalvular AF (NVAF) in tertiary reference centers across the country, along with an assessment of the compliance of these practices with international AF management guidelines. In addition, outcomes of thromboprophylaxis and the quality of life of the patients were evaluated.

METHODS

Study design and population

This was a representative, prospective, observational study conducted from August 2012 through November 2013 at 10 tertiary healthcare centers across the country. The study did not include any intervention in routine clinical practice. Consecutive patients who were 18 years of age or older and diagnosed with NVAF (sustained arrhythmia lasting more than 30 seconds on electrocardiogram [ECG] or ECG-Holter monitoring) were included. Patients with cognitive disorders, postoperative NVAF, or NVAF due to reversible causes (e.g., pneumonia or hyperthyroidism), those who had myocardial infarction or underwent any operation within the previous 3 months, those who participated in another clinical trial in the previous 6 months, and pregnant or breastfeeding females were excluded. Moreover, patients with severe aortic valve stenosis and severe tricuspid valve stenosis were also not included in the analysis.

Abbreviations:

AF	*Atrial fibrillation*
$CHADS_2$	*Congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism*
CHA_2DS_2-VASc	*Congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65 to 74 years, female*
ECG	*Electrocardiogram*
HAS-BLED	*Hypertension, abnormal renal or hepatic function, stroke, bleeding, labile international normalized ratio, age ≥65 years, drugs or alcohol*
INR	*International normalized ratio*
NVAF	*Nonvalvular AF*
TTR	*Time in therapeutic range*

Written, informed consent was obtained from each patient before initiation of the study procedures. The study was approved by the ethics committee of Baskent University Ankara Hospital and conducted in accordance with the latest version of the Helsinki Declaration.

Data collected in the study visits and the measuring tools

As part of the study protocol, 3 visits were performed: a baseline clinical evaluation and a phone interview at the 6th and 12th month (phone visits). Thus, each patient was followed-up for 1 year in the study at 6-month intervals.

In the baseline visit, the following data were recorded: sociodemographic characteristics, type of AF, cardiovascular risk factors, history of coronary artery disease, concomitant diseases and treatments, agents used for stroke prevention (oral anticoagulant [warfarin, rivaroxaban, dabigatran, apixaban],

or antiplatelet agent), physical findings, and echocardiographic findings. Thereafter, patients were classified into the risk groups according the $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED scoring systems.[8–10] At the baseline clinical visit, all of the patients were given a diary to record information on AF treatment and INR results.

In follow-up phone visits, information on treatment course, side effects, persistence with initial treatment, INR results, hospital admissions, hospitalizations, and significant clinical events, such as stroke and bleeding, were collected. Patients were classified according to INR level of <2.0, 2.0–3.0, and ≥3.0. Time in therapeutic range (TTR) was calculated according to the Rosendaal method.[11] Percentage of time in the therapeutic INR (therapeutic TTR ≥60%) range of 2.0–3.0 and nontherapeutic INR range of <2 or ≥3 (nontherapeutic TTR <60%) were calculated for 1 year of follow-up.

The quality of life of the patients was assessed using the EuroQol 5-dimensional quality of life questionnaire (EQ-5D), for which validity and reliability have been performed.[12] The EQ-5D was completed at the baseline visit and in the telephone interview at the 12th month.

Statistical analysis

Data were analyzed using PASW Statistics for Windows, Version 18 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as numbers and percentages for categorical variables, and mean, standard deviation, median, and minimum and maximum values for numerical variables. Visual (histogram and probability graphs) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk tests) methods were used to test the normality of variables. If no more than 20% of the cells had expected frequencies less than 5, a chi-square test was used, and if not, Fisher's exact test was used for 2-group comparisons, and for multiple group comparisons, Fisher's exact test was used. The McNemar test was used for paired group comparisons of dependent categorical variables. For non-normally distributed numerical variables, the Mann-Whitney U test was used to compare 2 independent groups and the Kruskal-Wallis test was used in the comparison of multiple independent groups. The Wilcoxon signed-rank test was used for paired group comparisons in the case of non-normal distribution of dependent numeric variables. The level of statistical significance was set at $p<0.05$.

RESULTS

Baseline characteristics

A total of 210 patients (120 males and 90 females; 129 inpatients and 81 outpatients; mean age: 64.86±12.87 years) with NVAF were included in the study. From the original 210 patients, follow-up data were collected through phone interviews for 146 patients (58.2% female) at the 6th month and for 140 patients (60.0% female) at the 12th month. At the baseline evaluation, most patients had high $CHADS_2$ (≥2: 48.3%) and CHA_2DS_2-VASc (≥2: 78.7%) risk scores, but low HAS-BLED scores (0–2: 83.1%). The mean baseline INR level of the patients was 2.15±0.88. In all, 41.8% (n=46) of the patients had an INR between 2.0 and 3.0. Heart valve regurgitation was recorded for 44.3% and 36.4% of patients in the mitral and tricuspid valves, respectively. The baseline clinical characteristics of the patients are summarized in Table 1.

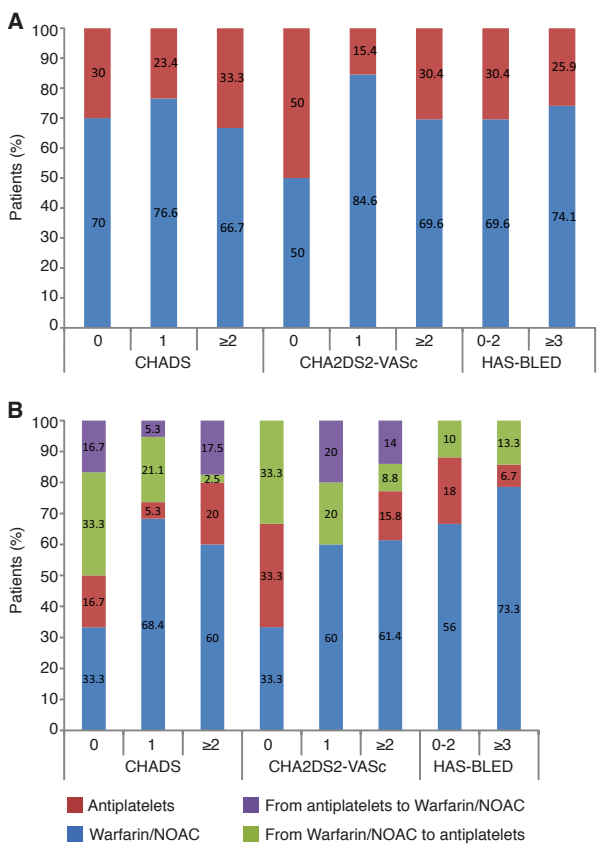

Figure 1. **(A)** Agents used at baseline, and **(B)** change in agent with respect to risk groups. P=0.509 for $CHADS_2$ risk groups, p=0.651 for HAS-BLED groups in Figure 1A. A p value could not be calculated for CHA_2DS_2-VASc in Figure 1b due to the limited number of cases.

Table 1. Baseline clinical and demographic characteristics of the patients (n=210)

Characteristics		Characteristics	
Age, years, mean±SD	64.86±12.87	Mild	80 (64.5)
Gender, n (%)		Moderate	39 (31.5)
Male	120 (57.1)	Severe	5 (4.0)
Female	90 (42.9)	Tricuspid valve failure	102 (36.4)
Type of hospital care, n (%)		Mild	68 (66.7)
Out patient	81 (38.6)	Moderate	25 (24.5)
In patient	129 (61.4)	Severe	9 (8.8)
Type of atrial fibrillation, n (%)		Aortic valve failure	37 (13.2)
Permanent	92 (43.8)	Mild	24 (66.7)
Paroxysmal	69 (32.9)	Moderate	13 (33.3)
Persistent	49 (23.3)	Severe	0
Risk stratification, n (%)		Mitral valve stenosis (mild)	9 (3.2)
$CHADS_2$		Mild	9 (100)
0	35 (16.9)	Moderate	–
1	72 (34.8)	Severe	–
≥2	100 (48.3)	Aortic valve stenosis	5 (1.8)
CHA_2DS_2-VASc		Mild	2 (40.0)
0	25 (12.1)	Moderate	1 (20.0)
1	19 (9.2)	Severe	2 (40.0)
≥2	163 (78.7)	Tricuspid valve stenosis	3 (1.1)
HAS-BLED		Mild	2 (66.7)
0-2	172 (83.1)	Moderate	1 (33.3)
≥3	35 (16.9)	Severe	–
International normalized ratio, n (%)		History of coronary artery disease, n (%)	
<2.0	47 (42.7)	Percutaneous coronary intervention	54 (26.6)
2.0-3.0	46 (41.8)	Acute coronary syndrome	37 (21.0)
≥3.0	17 (15.5)	Coronary bypass	24 (12.6)
Echocardiography findings, n (%)			
Mitral valve failure	124 (44.3)		

SD: Standard deviation. The percentages were calculated based on the patients who provided the relevant information.

Treatment and persistence with initial treatment

At baseline, 177 of 210 NVAF patients (84.3%) were not receiving any treatment for AF. At the 6th month, 141 (96.6%) of 146 patients were receiving treatment for AF, and at the 12th month, the figure was 136 (97.1%) of 140 patients. Approximately two-thirds of the patients who reported the type of antithrombotic in use were taking oral anticoagulants, and the remaining one-third were using antiplatelet agents (Table 2). The type of AF, the presence of bleeding, stroke, cardiovascular events, and survival status of patients had no significant relationship to the type of anticoagulant used ($p>0.05$ for all, Table 2). The risk group according to $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED score also had no significant effect on the choice of anticoagulant at baseline (oral anticoagulant versus antiplatelet) ($p>0.05$ for all, Fig. 1a). In 34 patients (26.4%) who were on antiplatelet treatment with CHA_2DS_2-VASc score of 2 or greater, the HAS-BLED score was calculated (data not shown).

The rate of persistence with the initial treatment was over 86% and no change in antithrombotic drug was recorded for approximately 21% of the patients in both 6-month and 12-month assessments (Table 3).

Table 2. Treatment with oral anticoagulants versus antiplatelet agents with respect to time, type of atrial fibrillation, the presence of clinical events, and survival

	Oral anticoagulants		Antiplatelet agents		*p*
	n	%	n	%	
Follow-up time					
Baseline	92	70.2	39	29.8	
6th month	86	74.1	30	25.9	
12th month	75	67.0	37	33.0	
Atrial fibrillation type					
Persistent	21	63.6	12	36.4	0.630
Permanent	52	72.2	20	27.8	
Paroxysmal	19	73.1	7	26.9	
Bleeding					
6^{th} month					
Yes	19	76.0	6	24.0	0.343
No	44	65.7	23	34.3	
12^{th} month					
Yes	22	75.9	7	24.1	0.519
No	50	69.4	22	30.6	
Stroke					
6^{th} month	4	100	0	0	NA
12^{th} month	2	50	2	50	NA
Cardiovascular events related to atrial fibrillation					
6^{th} month	4	80	1	20	NA
12^{th} month	1	33.3	2	66.7	NA
Survival					
Survived	84	91.3	33	84.6	0.353
Died	8	8.7	6	15.4	

The percentages were calculated based on the patients who provided the relevant information. NA: Not applicable as a result of the limited number of cases.

Fifty-nine patients (77.6%) were using the same antithrombotic at the baseline and at the 12^{th} month, while 8 patients (10.5%) changed from an oral anticoagulant to an antiplatelet, and 9 patients (11.8%) changed from an antiplatelet to an oral anticoagulant during the 12-month follow-up. The drug-change pattern revealed no association with $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED risk stratification (Fig. 1b). The most common reason for the change in anticoagulant drug was non-therapeutic TTR (n=9, 34.6%, cumulatively), followed by drug intolerance, bleeding, and other drug-related factors [12-month cumulative values: 6 (23.1%), 6 (23.1%) and 5 (19.2%), respectively] (Table 3).

Clinical course of disease during 12-month follow-up

During the 12-month follow-up, 44.3% of NVAF patients went to the hospital for INR control and 80% for other reasons. Overall, 15 patients were hospitalized in the first 6 months, and 8 patients in the second 6 months of the year of follow-up (Table 4). The most significant clinical event during the follow-up period was bleeding, which was reported by 22.6% and 25.0% of the patients in the 6- and 12-month phone interviews, respectively (Table 4). Only 8 patients reported major bleeding, including gastrointestinal, brain, lung, nasal, or urinary tract bleeding, at the 6-month visit, and 10 at the 12-month visit.

Table 3. Persistence with initial treatment and changes during treatment

	6-month follow-up (n=146)		12-month follow-up (n=140)		*p*
	n	%	n	%	
Drug continuance	122	86.5	118	86.8	0.727
Change in anticoagulant drug	26	21.3	25	21.4	0.815
Change in the dosage of anticoagulant agent	41	33.6	42	36.8	0.742
Reasons for the change in anticoagulant drug					
Outside the therapeutic INR range (TTR)	4	22.2	7	43.8	
Intolerance	3	16.7	4	25.0	
Bleeding	3	16.7	3	18.8	
Drug-related factors other than intolerance (i.e., ineffectiveness, price etc.)	8	44.4	2	12.5	
Addition of a new drug to the current anticoagulant treatment	61	50.0	88	75.2	<0.001

INR: International normalized ratio; TTR: Time in therapeutic range. The percentages were calculated based on the patients who provided the relevant information.

Table 4. Clinical course of disease for 1 year of follow-up with phone interviews at 6-month intervals

	6-month follow-up (n=146)		12-month follow-up (n=140)		*p*
	n	%	n	%	
Admission to the hospital for INR control	72	49.3	62	44.3	0.037
Admission to the hospital for reasons other than INR control	76	52.1	112	80.0	<0.001
Hospitalization	15	10.2	8	5.7	
Change in physician	52	35.6	73	52.1	0.002
Clinical events					
Bleeding*	33	22.6	35	25.0	
Stroke	6	4.1	5	3.6	
Others	19	13	16	11.4	
Cardiovascular events related to atrial fibrillation	9	6.2	7	5	
Cardiovascular events not related to atrial fibrillation	12	8.2	5	3.6	
None	68	46.6	75	53.6	
Death	15	9.3	5	3.4	

INR: International normalized ratio. *Brain bleeding, urinary tract bleeding, bowel bleeding, gingival bleeding, nasal bleeding, bleeding due to simple or serious trauma etc., except for menstrual bleeding. At 6-month and 12-month follow-up interviews, 8 and 10 patients reported major bleeding, respectively. The percentages were calculated based on the patients who provided the relevant information.

HAS-BLED category demonstrated no relationship to bleeding events. The HAS-BLED score was ≥3 in 26.4% (n=14) of the patients with bleeding and in 13.5% (n=10) of those without bleeding (p=0.067) (data not shown). Of the patients who used warfarin initially and at the 12th month, 48.6% had a bleeding complication. There was also no difference in the bleeding rate between the patients who used or started

Table 5. INR of patients with respect to evaluation time, presence of clinical event, bleeding, stroke, and hospitalization

	INR <2.0		INR 2.0–3.0		INR ≥3.0		*p*
	n	%	n	%	n	%	
Total							
6th month	7	20.0	23	65.7	5	14.3	
12th month	11	25.0	29	65.9	4	9.1	
Clinical event							
6th month							
Yes	3	13.6	15	68.2	4	18.2	0.403
No	4	30.8	8	61.5	1	7.7	
12th month							
Yes	6	22.2	18	66.7	3	11.1	NA
No	5	29.4	11	64.7	1	5.9	
Bleeding							
6th month							
Yes	2	18.2	7	63.6	2	18.2	1.000
No	5	20.8	16	66.7	3	12.5	
12th month							
Yes	2	14.3	9	64.3	3	21.4	NA
No	9	30.0	20	66.7	1	3.3	
Stroke							
6th month							
Yes	1	33.3	2	66.7	0	0.0	NA
No	6	18.8	21	65.6	5	15.6	
12th month							
Yes	2	66.7	1	33.3	0	0.0	
No	9	22.0	28	68.3	4	9.8	
Hospitalization							
6th month							
Yes	0	0.0	6	85.7	1	14.3	NA
No	4	26.7	8	53.3	3	20.0	
12th month							
Yes	4	23.5	10	58.8	3	17.6	NA
No	6	24.0	18	72.0	1	4.0	

INR: International normalized ratio. The percentages were calculated based on the patients who provided the relevant information. The analysis was performed using the data of patients with laboratory analysis results from within the previous 2 months. NA: Not applicable as a result of the limited number of cases.

to use warfarin and those who did not use or discontinued warfarin (42.9% vs. 43.9%; p=0.917) (data not shown).

Around half of the patients had no clinical event. Twenty patients died during the 12-month follow-up (Table 4). There was no correlation between mortality and warfarin treatment: 7 of 92 patients (7.6%) who used warfarin at baseline died, while 13 of 118 (11.0%) who did not use warfarin at baseline died during the follow-up period (p=0.404) (data not shown). The mortality rate was not significantly higher in the patients who were not using warfarin initially and

Table 6. Rate of therapeutic or non-therapeutic time in therapeutic range for 1 year of follow-up

	Therapeutic TTR	Non-Therapeutic TTR	*p*
Total	36 (61.0)	23 (39.0)	
Bleeding			
Yes	17 (65.4)	9 (34.6)	0.569
No	15 (57.7)	11 (42.3)	
Stroke			
Yes	2 (40.0)	3 (60.0)	0.361
No	30 (63.8)	17 (36.2)	
Clinical event			
Yes	25 (59.5)	17 (40.5)	0.626
No	10 (66.7)	5 (33.3)	
Drug groups	30 (66.7)	15 (33.3)	NA
Oral anticoagulants*			
Antiplatelet agents	1 (33.3)	2 (66.7)	
Cardiovascular events related to atrial fibrillation	2 (66.7)	1 (33.3)	

TTR: Time in therapeutic range. The percentages were calculated based on the patients who provided the relevant information. Therapeutic TTR (≥60%) corresponds to normal INR level (INR=2-3); Non-therapeutic TTR (<60%) corresponds to INR <2 or INR≥3. *Of the patients using oral anticoagulants, all were taking warfarin. INR: International normalized ratio; NA, not applicable as a result of the limited number of cases.

then changed drug (11/92, 12.0%) than those who were using warfarin at baseline and then changed drug (9/118, 7.6%) (p=0.289) (data are not shown).

Change in international normalized ratio during follow-up

The percentage of patients with the target INR (2.0 to 3.0), which was 41.8% at baseline, increased to 65.7% at the 6th month and 65.9% at the 12th month (Table 5). The presence of a clinical event, bleeding, stroke, or hospitalization was not significantly related to the ratio of patients with the target INR (p>0.05 for all, Table 5). The therapeutic TTR was 61.0% during the year of follow-up. The mean TTR was 65.9±32.6%. The presence of bleeding, stroke, or clinical event did not affect the therapeutic TTR (p>0.05 for all, Table 6). The relationship between anticoagulant drug group and therapeutic TTR could not be evaluated due to the limited number of cases (Table 6).

Quality of life

The median EQ-5D score of the patients at baseline and at the 12th month was 0.827 (range: 0.145–1.000) and 0.778 (range: -0.040–1.000) (p<0.001), respectively. Thus, the quality of life of patients declined over time. The EQ-5D score did not indicate a significant difference with respect to the type of AF, drug group, or presence of bleeding at baseline and the 12th month (Table 7). However, the quality of life of the patients who used oral anticoagulants significantly worsened over time. The EQ-5D scores of patients who used antiplatelet agents also deteriorated over time without a significant difference (Table 7). While the presence of bleeding or any clinical event had no effect on EQ-5D score at baseline (p=0.873 and p=0.402), patients with a bleeding complication or a clinical event had significantly lower scores than those without at the 12th month (p=0.018 and p=0.011, respectively). The quality of life of the patients with bleeding became poorer over time. The EQ-5D score of patients who were treated with an oral anticoagulant during the 12-month follow-up also decreased significantly (p=0.006; Table 7).

DISCUSSION

Drug treatment in AF aims to reduce the risk of AF-related severe thromboembolic events[7,13] and this is basically managed with antithrombotic therapy (anticoagulant). However, such therapy is associated

Table 7. EuroQol 5-dimensional questionnaire scores of the patients at baseline and 12th month

	Baseline	12th month	p
Total	0.827 (0.145–1.000)	0.778 (-0.040–1.000)	<0.001
Type of atrial fibrillation			
Persistent	0.843 (0.543–1.000)	0.770 (0.193–1.000)	<0.001
Permanent	0.805 (0.145–1.000)	0.681 (-0.040–1.000)	<0.001
Paroxysmal	0.833 (0.333–1.000)	0.827 (0.077–1.000)	0.040
p	0.117	0.043	
Drug groups			
Oral anticoagulants	0.827 (0.333–1.000)	0.728 (0.165–1.000)	0.003
Antiplatelet agents	0.705 (0.145–1.000)	0.699 (-0.040–1.000)	0.333
p	0.219	0.815	
Bleeding			
Yes	0.833 (0.597–1.000)	0.689 (-0.040–1.000)	<0.001
No	0.835 (0.165–1.000)	0.800 (0.165–1.000)	0.001
p	0.873	0.018	
Clinical event			
Yes	0.827 (0.165–1.000)	0.742 (-0.040–1.000)	<0.001
No	0.844 (0.543–1.000)	0.800 (0.235–1.000)	0.045
p	0.402	0.011	
Drug usage pattern throughout the study			
Oral anticoagulant	0.816 (0.165–1.000)	0.755 (0.165–1.000)	0.006
Antiplatelet agents	0.757 (0.597–1.000)	0.800 (-0.040–1.000)	NA
Oral anticoagulant →Antiplatelet	1.000 (0.597–1.000)	0.742 (0.397–1.000)	NA
Antiplatelet→Oral anticoagulant	0.794 (0.308–1.000)	0.499 (0.165–1.000)	NA

EuroQol 5-dimensional questionnaire (EQ-5D) scores of the patients who were followed-up in both the 6th and 12th months were analyzed. For bleeding and clinical event, cumulative data were used. For analysis of EQ-5D scores in drug groups, only the data of the patients using the same drug throughout the study were included. NA: Not applicable as a result of the limited number of cases.

with an increased risk of bleeding; thus, both the benefit and the risk should be taken into account in AF treatment planning. Many clinical trials [SPAF (Stroke Prevention in Atrial Fibrillation), AFASAK (Atrial Fibrillation, Aspirin, Anticoagulation Therapy Study), BAATAF (Boston Area Anticoagulation Trial in Atrial Fibrillation), SPINAF (Stroke Prevention in Nonrheumatic Atrial Fibrillation), and CAFA (Canadian Atrial Fibrillation Anticoagulation)] have demonstrated that warfarin significantly reduces the incidence of stroke compared with a placebo in patients with AF at moderate to high risk of thromboembolic events (CHA_2DS_2-VASc score ≥2).[14–19] The risk of serious bleeding, however, doubles with warfarin anticoagulation. In addition to oral anticoagulants, various antiplatelet regimens have been studied, but no clinical benefit over warfarin has been demonstrated for these regimens.[20,21] Therefore, oral anticoagulant use is currently the gold-standard antithrombotic regimen for NVAF. Although international guidelines have been developed for risk assessment and stroke prevention of AF, the implementation of the guidelines has not been fully realized and real-life practice may include variations in different health care settings.

In this study conducted at tertiary reference centers, only two-thirds of the patients were taking oral anticoagulants and the remaining one-third were on antiplatelet agents. Similarly, in the RAMSES (Real-life Multicentre Survey Evaluating Stroke Prevention Strategies) study,[22] the largest study in Turkey evaluating stroke prevention strategies in NVAF patients (n=6273), 72% and 32% of the study population were on oral anticoagulants and antiplatelet agents, respec-

tively. One striking finding of the present study was that although the majority of the patients were stratified with respect to risk for stroke and bleeding according to $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED scores, the selection of antithrombotic treatment was not based on the stroke or bleeding risk score of the patients. Oral anticoagulants are recommended for patients with NVAF with a CHA_2DS_2-VASc score of 2 or greater.[4,7] Although 78.7% of the patients had CHA_2DS_2-VASc score of 2 or greater, only 66.7% of these high-risk patients were treated with oral anticoagulants. On the other hand, the oral anticoagulant treatment rate was 70% and 76.6% in patients with a CHA_2DS_2-VASc score of 0 and 1, respectively. Likewise, in the RAMSES study,[22] the rate of oral anticoagulant use was reported as 72% for patients with CHA_2DS_2-VASc scores of both 0 and 1. Thus, contrary to the guideline recommendations, oral anticoagulants were underutilized in patients with high stroke risk, while they were overutilized in patients with low risk.

HAS-BLED has been shown to better predict bleeding risk in AF patients compared with other assessment tools.[23,24] A HAS-BLED score of 3 or greater is considered to be an indicator of a high bleeding risk. At initial evaluation, 16.9% of our study population had a HAS-BLED score of 3 or greater. However, of these patients with high bleeding risk, 74.1% and 73.3% were receiving oral anticoagulant treatment at baseline and at the 1-year follow-up, respectively, without any significant effect of HAS-BLED scoring on treatment choice. Thus, HAS-BLED was not commonly used in clinical practice to evaluate bleeding risk before initiation of antithrombotic therapy.

The WARFARIN TR study,[25] which was conducted with an adult Turkish population (n=4987) using warfarin and undergoing regular INR monitoring, reported that the rate of patients with target INR in the therapeutic range was 24.6%. In our series, the antithrombotic treatment and persistence with initial treatment rates were over 85% and TTR was 61.0% at the 1-year follow-up. The rate of patients with the target INR (2.0 to 3.0) increased to 65.7% at the 6th month, and 65.9% at the 12th month from 41.8% at the baseline.

The bleeding rate was quite high: 22.6% and 25.0% in the 6- and 12-month evaluation, respectively. It should also be noted that HAS-BLED category had no association with bleeding events in our study. In the WARFARIN TR study,[25] the bleeding rate within a year was reported to be 20.1%.

One of the limitations of the present study was the inclusion of patients only from tertiary healthcare centers; patients may have been admitted for complex procedures. In addition, potential changes to the reimbursement system of the Social Security Institute may have resulted in changes in clinical practice after the present study.

In conclusion, oral anticoagulants are underused and antiplatelets are prescribed for a significant number of patients, even at tertiary reference centers. Despite the high probability of treatment and persistence with initial treatment, the outcome of thromboprophylaxis as well as patient quality of life were not at the desired level. Thus, we suggest that health policies at national level should be developed and implemented to better integrate international guidelines for the management of NVAF into clinical practice.

The present study was presented as a poster in the International Society for Pharmacoeconomics and Outcomes Research 17th Annual European Congress, held on November 8–12, 2014 in Amsterdam, Netherlands.

Peer-review: Externally peer-reviewed.

Funding: The present study was supported by Pfizer Pharmaceuticals Turkey and Bristol-Myers Squibb Turkey.

Conflict of interest: Bülent Özin, Kudret Aytemir, Özgür Aslan, Türkay Özcan, Mehmet Kanadaşı, Mesut Demir, Mustafa Gökçe, Mehmet Murat Sucu, Murat Özdemir, Zerrin Yiğit, Mustafa Ferzeyn Yavuzkır, and Ali Oto received reserch grant from Pfizer Pharmaceuticals Turkey and Bristol-Myers Squibb Turkey.

Authorship contributions: Concept: All; Design: All; Supervision: A.O.; Materials: All; Data Collection & Processing: All; Analysis and interpretation: All; Literature search: Pfizer /Bristol Myers; Writing: A.O., B.Ö.; Critical revisions: A.O., B.Ö.

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Keywords: Anticoagulants; atrial fibrillation; quality of life in atrial fibrillation; treatment outcome in atrial fibrillation; warfarin.

Anahtar sözcükler: Antikoagulan; atriyum fibrilasyonu; yaşam kalitesi; tedavi sonuçları; warfarin.