

Comparison of health-related quality of life among patients using novel oral anticoagulants or warfarin for non-valvular atrial fibrillation

Kevser Gülcihan Balcı, Mustafa Mücahit Balcı, Uğur Canpolat, Fatih Şen, Mehmet K. Akboğa, Muhammed Süleymanoğlu, Serdar Kuyumcu, Orhan Maden, Hatice Selçuk, Mehmet Timur Selçuk

Department of Cardiology, Türkiye Yüksek İhtisas Research and Education Hospital; Ankara-Turkey

ABSTRACT

Objective: The aim of this study was to compare health-related quality of life (HRQoL) measures between novel oral anticoagulants (NOACs) and warfarin-treated Turkish patients who had been started on oral anticoagulants (OACs) due to non-valvular atrial fibrillation (AF) and to determine the effects of OACs on patient's emotional status, anxiety and depression.

Methods: A total of 182 patients older than 18 years with non-valvular AF and being treated with OACs for at least 6 months according to current AF guidelines who were admitted to outpatient clinics between July 2014 and January 2015 were included in this cross-sectional study. The exclusion criteria were receiving OACs for conditions other than non-valvular AF and being unable to answer the questionnaire. A questionnaire was administered to all participants to evaluate HRQoL, depression and anxiety. The mean differences between the groups were compared using Student's t-test; the Mann-Whitney U test was applied for comparisons of the medians.

Results: The annual number of hospital admissions was significantly higher in the warfarin group ($p<0.001$), and all HRQoL scores were significantly lower and Hospital Anxiety and Depression Scale (HADS) score was higher in the warfarin group ($p<0.001$). History of any type of bleeding was significantly higher in the warfarin group ($p<0.001$). However, none of the patients had major bleeding. Among patients who experienced bleeding, all HRQoL scores were significantly lower and HADS score was significantly higher ($p<0.001$ and $p=0.002$, respectively).

Conclusion: Warfarin-treated patients had higher levels of self-reported symptoms of depression and anxiety and compromised HRQoL when compared with NOAC-treated patients. The results may be explained by higher rates of bleeding episodes and higher number of hospital admissions, which may cause restrictions in life while on warfarin treatment. (*Anatol J Cardiol* 2016; 16: 474-81)

Keywords: atrial fibrillation, warfarin, apixaban, dabigatran, quality of life, anxiety

Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice that has been shown to be significantly associated with increased morbidity and mortality (1). As a major cardiovascular challenge in the general population, it should be evaluated by its medical, social and economic aspects. Medical management of AF patients primarily focuses on the alleviation of AF-related symptoms and prevention of severe complications associated with AF, such as thromboembolism. In order to prevent AF-related complications, antithrombotic therapy, control of ventricular rate and treatment of concomitant cardiac diseases should be initiated in parallel to each other (2). Among the various antithrombotic and anticoagulant agents, vitamin K antagonists (VKAs) and novel oral anticoagulants (NOACs) are recommended by most recent AF guidelines (3, 4).

VKAs have been prescribed for many years for the prevention of thromboembolic events in both valvular and non-valvular AF (2-4). However, usage of VKAs is complicated due to highly variable biological effects and their narrow therapeutic index (5, 6). Thus, patients who have been treated with VKAs require more frequent outpatient visits for monitoring the international normalised ratio (INR) and also dietary restrictions to lower vitamin K intake that has a negative impact on health-related quality of life (HRQoL) among patients (7). Clinical studies have primarily focused on evaluation of the efficacy and safety of anticoagulant therapy but not on HRQoL. NOACs have been developed in recent years that may offer some solution to problems with respect to efficacy, safety and HRQoL (8). They do not require any periodic blood monitoring for efficacy. Also, they exhibit a wide therapeutic window and low inter- and intra-individual variability in the dose-effect relation with fewer drug interactions (8). Therefore, patient's perception of HRQoL may differ according to the type of oral anticoagulant (OAC) used.

Address for Correspondence: Dr. Kevser G. Balcı, Park Flora Sitesi B Blok No:4
Yaşamkent Çay yolu, 06810, Ankara-Türkiye
Phone: +90 530 328 38 69 Fax: +90 312 306 10 00 E-mail: kevs84@gmail.com

Accepted Date: 13.05.2015 **Available Online Date:** 14.07.2015

© Copyright 2016 by Turkish Society of Cardiology - Available online at www.anatoljcardiol.com
DOI:10.5152/AnatolJCardiol.2015.6334



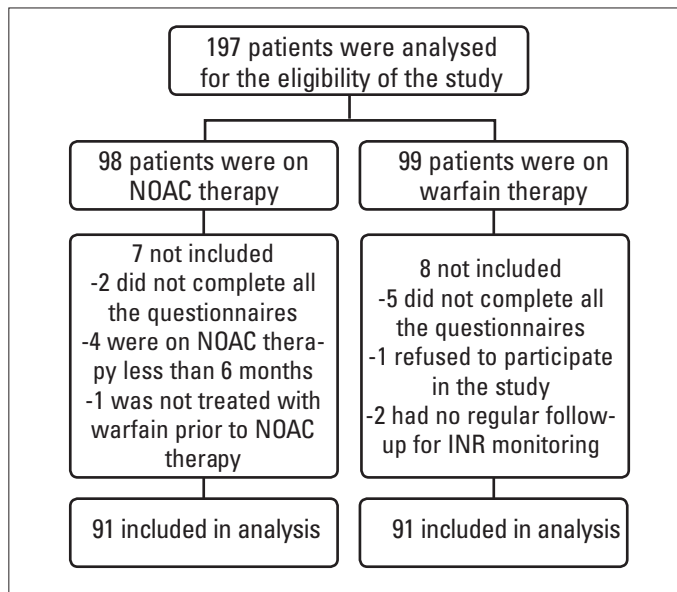


Figure 1. Flowchart of the study

Therefore, the aim of our study was to compare HRQoL among Turkish patients in whom oral anticoagulation with VKAs or NOACs have been initiated for non-valvular AF and also to assess the impact of OACs on patient's emotional status, anxiety and depression.

Methods

In this cross-sectional study, a total of 182 patients (mean age: 65.5 ± 10.1 years, 49% male) who admitted to our outpatient clinic peculiar to anticoagulated patients were included between July 2014 and January 2015 (Fig. 1). A questionnaire was administered to all participants to evaluate their HRQoL. The inclusion criteria were as follows: age ≥ 18 years, previous diagnosis of non-valvular AF, having an indication for OACs according to the current AF guidelines and being treated with OACs for at least 6 months. Patients receiving OACs for valvular AF, mechanical heart valve prosthesis or venous thromboembolism and those who were unable to answer the questionnaire because of cooperation problems were excluded from the study. The study population was categorised into two groups: the 'warfarin group' or the 'NOAC group'. In the NOAC group, all patients were treated with warfarin previously and the clinician switched to NOACs at least 6 months ago because of the labile INRs or complications with VKAs. The median time from prior warfarin usage in the NOAC-treated group was 25 (14–52) months. In the NOAC group, the patients were on dabigatran, apixaban or rivaroxaban treatment, which are approved in Turkey for the prophylaxis of embolism in AF.

The primary outcome of the study was the incidence of bleeding. A total sample size of 162 patients (81 per group) was required to detect at least 20% difference with 80% power at 5% significance level. The difference of 20% was taken from both a

pilot study and clinical experience. Sample size estimation was performed using NCSS and PASS 2000 software (Number Cruncher Statistical Systems, Kaysville, Utah, USA). Major bleeding was defined as fatal and symptomatic bleeding and/or any bleeding requiring blood transfusion and/or 3 g/dL or more decrease in haemoglobin levels while on OAC treatment (9), as determined from the electronic medical records or self-report by the patient. The INR was calculated by raising the prothrombin time ratio (PT of a test sample compared with normal PT) to the power of a coefficient known as the international sensitivity index. The intended INR for non-valvular AF was 2.0–3.0. INR stability was calculated using the INR number within the therapeutic range divided by the collected INR number (for instance, follow-up INR levels for a patient - INR1=1.4, INR2=1.8, INR3=2.5, INR4=2.95, INR5=4.7: 2 values within the target level, presented 40% stability). The annual number of hospital admissions was calculated as follows: (all admissions that were only OAC related since the OAC-therapy first started $\times 12$) / (duration of OAC therapy in months). Each interview lasted approximately 20 min. Electronic medical records were also used to obtain socio-demographic and clinical data of participants. All patients gave informed consent, and the study protocol was approved by the institutional Ethics Committee.

CHA₂DS₂-VASc, HAS-BLED and EHRA scores

All patients were evaluated with the original scoring system to calculate the CHA₂DS₂-VASc score: congestive heart failure (1 point); history of hypertension (1 point); age (≥ 75 years, 2 points; >65 to <75 years, 1 point); diabetes mellitus (1 point); history of stroke, transient ischemic attack (TIA), peripheral embolic event (2 points); vascular disease (1 point); female gender (1 point) (2). Bleeding risk was assessed using the HAS-BLED score: hypertension (1 point), abnormal renal/liver function (1 point each), stroke (1 point), bleeding history or predisposition (1 point), labile INR (1 point), elderly (>65 years, 1 point), drugs/alcohol concomitantly (1 point each) (2). The European Heart Rhythm Association (EHRA) score was used to assess the severity of AF-related symptoms (2): EHRA I: No symptoms; II: 'Mild symptoms', normal daily activity not affected; III: 'Severe symptoms', normal daily activity affected and IV: 'Disabling symptoms', normal daily activity discontinued.

Questionnaire

A questionnaire consisting of open-ended questions was given to the patients during routine outpatient clinic visits. HRQoL was measured using the self-reported questions of the Medical Outcomes Study Form 36 (SF-36), which is composed of 8 subscales that reflect both physical health [physical functioning (PF), role-physical (RP), bodily pain (BP) and general health (GH)] and mental health [vitality (VT), social functioning (SF), role emotional (RE) and mental functioning (MF)] (10). Scores ranging from 0 to 100 were obtained, and higher scores indicate better functioning with fewer problems. The Hospital Anxiety and

Table 1. Baseline characteristics of the study groups (n=182)

Variables	Warfarin group (n=91)	NOAC group (n=91)	P
Age, years, mean±SD	64.8±10.2	66.2±10.1	0.347 [†]
Female gender	48 (52.7%)	43 (47.3%)	0.459 [‡]
Education level			
Uneducated	17 (18.7%)	24 (26.4%)	0.273 [‡]
Primary school	66 (72.5%)	63 (69.2%)	
Middle and high school	8 (8.8%)	4 (4.4%)	
Marital status			
Married	80 (87.9%)	68 (74.7%)	0.022 [‡]
Unmarried (single, divorced or widowed)	11 (12.1%)	23 (25.3%)	
Duration of OAC therapy (m)	20 (9–38)	9 (7–12.5)	<0.001 [¶]
Medication			-
Warfarin	91 (100%)	-	
Dabigatran 150 mg bid	-	37 (40.7%)	
Dabigatran 110 mg bid	-	10 (11.0%)	
Rivaroxaban 20 mg od	-	16 (17.6%)	
Apixaban 5 mg bid	-	26 (28.6%)	
Apixaban 2.5 mg bid	-	2 (2.2%)	
LVEF, %	55 (15–65)	60 (15–60)	0.267 [¶]
Hypertension, n (%)	67 (73.6%)	66 (72.5%)	0.867 [‡]
Coronary artery disease, n (%)	54 (59.3%)	38 (41.8%)	0.018 [‡]
Diabetes mellitus, n (%)	17 (18.7%)	18 (19.8%)	0.851 [‡]
Heart failure, n (%)	27 (29.7%)	25 (27.5%)	0.743 [‡]
CHA2DS2–VASc, median	3 (1–8)	3 (1–7)	0.421 [¶]
MC (MMAS-4 scores of <2, n (%))	70 (76.9%)	78 (85.7%)	0.128 [‡]
AN of hospital admissions, mean±S.D.	12.8±3.5	5.0±1.3	<0.001 [†]
EHRA score, median, min–max			
1	34 (37.4%)	54 (59.3%)	0.010 [¶]
2	44 (48.4%)	26 (28.6%)	
3	13 (14.3%)	10 (11.0%)	
4	0 (0.0%)	1 (1.1%)	
HAS-BLED score			
0–2	72 (79.1%)	68 (74.7%)	0.824 [¶]
≥3	19 (20.9%)	23 (25.3%)	

[†]Student's t-test, [‡]Pearson chi-square test, [¶]Mann–Whitney U test; AN: annual number, CHA2DS2–VASc: congestive heart failure, history of hypertension, age, diabetes mellitus, history of stroke/TIA/embolic event, vascular disease, female gender; EHRA - European Heart Rhythm Association; HAS-BLED - hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalised ratio, elderly, drug/alcohol use; LVEF - left ventricular ejection fraction; m: months; MC - medical compliance; MMAS - Morisky Medication Adherence Scale; NOAC - novel oral anticoagulant

Depression Scale (HADS) was used to determine the depression and anxiety scores of the patients (11). The HADS consists of 14 items that include a 7-item depression scale (HADS-D) and a 7-item anxiety scale (HADS-A). Anxiety scores were evaluated over 21 points; scores ranging from 8 to 10 points were considered as having tendency for anxiety, whereas scores of 10 or more points were considered as having anxiety (12). As for depression, scores were evaluated over 21 points; 5–7 points were consid-

ered as having tendency for depression, whereas scores greater than 7 points were considered as having depression (12). The Morisky Medication Adherence Scale (MMAS) was used to determine medical compliance (13); patients with MMAS-4 scores of <2 were considered as highly adherent and compliant with OAC treatment in our study. Uneducated patients answered the questionnaire with the help of an educated relative or a doctor without any manipulation.

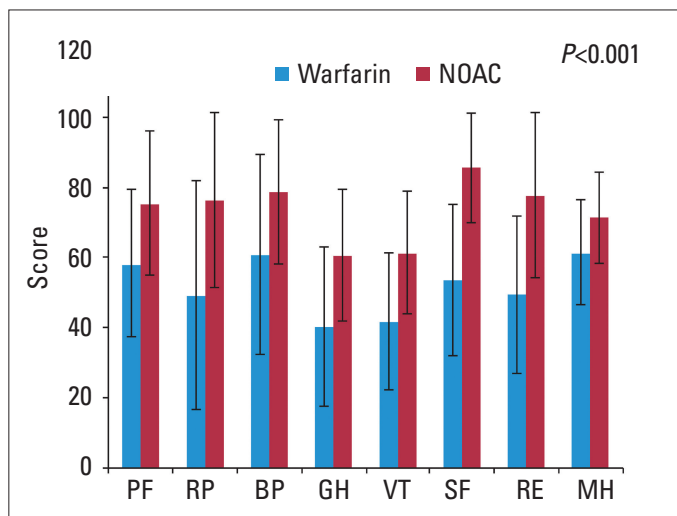


Figure 2. Comparison of health-related quality of life measures between the study groups

BP - bodily pain; GH - general health; MF - mental functioning; NOAC - novel oral anticoagulant; PF - physical functioning; RE - role emotional; RP - role-physical; SF - social functioning; VT - vitality

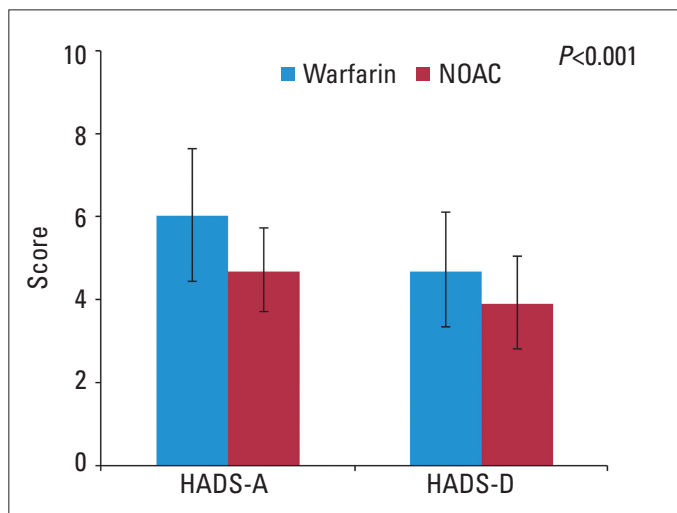


Figure 3. Comparison of Hospital Anxiety and Depression Scale scores between the study groups

HADS - Hospital Anxiety and Depression Scale; HADS-A - anxiety subscale of HADS; HADS-D - depression subscale of HADS; NOAC - novel oral anticoagulant

Statistical analysis

Data analysis was performed using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, US). Data were shown as mean±SD or median (min-max), where applicable. The mean differences between the groups were compared using Student's t-test; the Mann-Whitney U test was applied for comparisons of medians. Nominal data were analysed by Pearson's chi-square test. Degrees of association between continuous variables were evaluated using Spearman's rank correlation analyses.

Whether the differences in HRQoL, HADS-A and HADS-D scores and annual number of hospital admissions between the warfarin and NOAC groups were to be continued or not were evaluated by analysis of covariance (ANCOVA) after adjustment

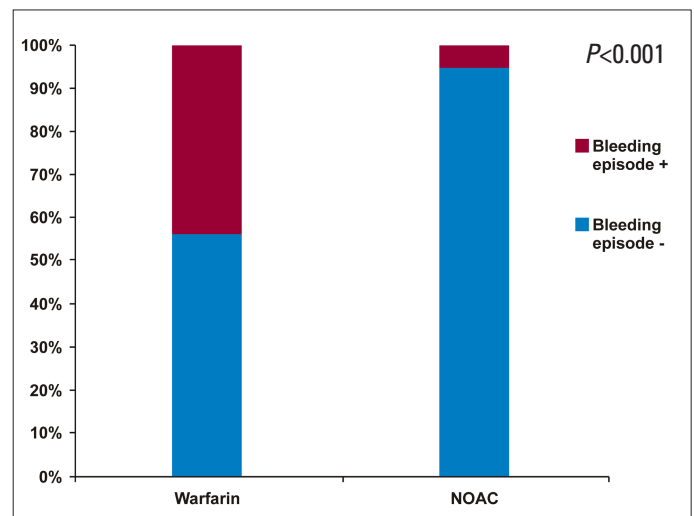


Figure 4. Comparison of the percentage of patients who experienced a bleeding episode between the study groups

NOAC - novel oral anticoagulant

for age, gender, time interval for anticoagulation and medical compliance. Multiple logistic regression analysis was applied for determining the difference between the warfarin and NOAC groups for bleeding after adjustment for all possible confounding factors (i.e. age, gender, anticoagulation time and medical compliance). Odds ratios and 95% confidence intervals for each independent variable were also calculated. A two-sided p value of <0.05 was considered statistically significant.

Results

The baseline characteristics of the study population are shown in Table 1. The socio-demographic and clinical parameters were similar between the study groups except for marital status and history of coronary artery disease ($p=0.022$ and $p=0.018$; respectively). CHA₂DS₂-VASc and HAS-BLED scores did not differ between the study groups ($p=0.421$ and $p=0.824$, respectively). The duration of OAC therapy was significantly longer in the warfarin group than in the NOAC group ($p<0.001$), and the annual number of hospital admissions was significantly higher in the warfarin group ($p<0.001$). Among warfarin-treated patients, only 24 (27%) showed INR stability up to 50% and 10 (11%) presented stability of 75% or above. Of these patients, 34 (37.3%) patients had effective INR levels.

All HRQoL scores (PF, RP, BP, GH, VT, SF, RE and MF) were significantly lower and HADS-A/HADS-D scores were higher in the warfarin group ($p<0.001$) (Fig. 2, 3). Correlation analysis revealed that there was a significant negative correlation between EHRA scores and HRQoL scores (PF, $r=-0.624$; RP, $r=-0.507$; BP, $r=-0.532$; GH, $r=-0.558$; VT, $r=-0.451$; SF, $r=-0.481$; RE, $r=-0.376$ and MF, $r=-0.375$; $p<0.001$), but no relationship was observed between EHRA and HADS scores ($p>0.05$). The annual number of hospital admissions showed a negative correlation with all HRQoL scores and a positive correlation with HADS-A

Table 2. Correlation analysis showing the association of quality of life, anxiety and depression levels with EHRA score and annual number of hospital admissions

	EHRA score		Annual number hospital admissions	
	R	p†	R	p†
Physical functioning	-0.624	<0.001	-0.375	<0.001
Role physical	-0.507	<0.001	-0.410	<0.001
Bodily pain	-0.532	<0.001	-0.328	<0.001
General health	-0.558	<0.001	-0.371	<0.001
Vitality	-0.451	<0.001	-0.402	<0.001
Social functioning	-0.481	<0.001	-0.600	<0.001
Role emotional	-0.376	<0.001	-0.493	<0.001
Mental functioning	-0.375	<0.001	-0.269	<0.001
HADS-A	-0.073	0.326	0.397	<0.001
HADS-D	0.018	0.813	0.260	<0.001

†Spearman's correlation analysis; EHRA - European Heart Rhythm Association; HADS - Hospital Anxiety and Depression Scale; HADS-A - Anxiety subscale of HADS; HADS-D - Depression subscale of HADS

Table 3. Comparison of unfavourable effects of oral anticoagulant therapies (n=182)

Variables	Warfarin group (n=91)	NOAC group (n=91)	P
History of bleeding, n (%)	40 (44.0%)	5 (5.5%)	<0.001‡
Type of bleeding, n (%)			-
Gingival bleeding	10 (11.0%)	1 (1.1%)	
Bruising	13 (14.3%)	1 (1.1%)	
Melena	2 (2.2%)	-	
Haematuria	4 (4.4%)	-	
Epistaxis	11 (12.1%)	3 (3.3%)	

‡Pearson chi-square test, NOAC - Novel oral anticoagulant

and HADS-D scores (PF, $r=-0.375$; RP, $r=-0.410$; BP, $r=-0.328$; GH, $r=-0.371$; VT, $r=-0.402$; SF, $r=-0.600$; RE, $r=-0.493$; ME, $r=-0.269$; HADS-A, $r=0.397$ and HADS-D, $r=0.260$; $p<0.001$) (Table 2). History of any type bleeding after starting OAC therapy was significantly higher in the warfarin group than in the NOAC group ($p<0.001$) (Fig. 4). However, none of patients had major bleeding (Table 3). In the warfarin-treated group, all bleeding episodes occurred when INR levels were ≥ 2.5 . At the time of the bleeding episode, there was no concomitant trauma and/or intervention and median INR was 3.7 (2.5–6.0). Among patients who experienced bleeding, all HRQoL scores were significantly lower and the HADS-D score was significantly higher ($p<0.001$ and $p=0.002$, respectively) (Table 4). When patients were analysed according to having effective INR levels, none of the HRQoL scores showed any significant difference between the groups ($p>0.05$); however, higher HADS-A and HADS-D scores were observed in the ineffective INR level

Table 4. Comparison of quality of life, anxiety and depression levels of patients according to the occurrence of any type bleeding event (n=182)

Variables	Bleeding (-) (n=137)	Bleeding (+) (n=45)	p†
Physical functioning	71.3±21.2	53.1±20.5	<0.001
Role physical	70.8±28.0	38.3±31.3	<0.001
Bodily pain	75.5±23.3	52.2±27.6	<0.001
General health	55.9±20.6	34.2±22.8	<0.001
Vitality	55.4±19.8	39.6±19.9	<0.001
Social functioning	76.2±21.3	49.2±23.4	<0.001
Role emotional	69.3±25.6	45.9±23.9	<0.001
Mental functioning	68.6±14.5	59.6±14.1	<0.001
HADS-A	5.3±1.4	5.5±1.5	0.352
HADS-D	4.2±1.3	4.8±1.3	0.002

†Student's t-test, HADS - Hospital Anxiety and Depression Scale; HADS-A - Anxiety subscale of HADS; HADS-D - Depression subscale of HADS

group [HADS-A: 5 (3–8) vs. 4 (3–7), $p=0.003$; HADS-D: 4 (2–6) vs. 3 (2–6), $p=0.013$].

After covariance adjustment for age, gender, duration of OAC therapy and drug compliance, all HRQoL scores were still significantly lower in the warfarin group ($p<0.05$), and HADS scores and the annual number of hospital admissions were significantly higher in the warfarin group ($p<0.001$) (Table 5). In multivariate logistic regression analysis, after adjustment according to the age, gender, duration of OAC therapy and drug compliance, usage of warfarin (OR: 31.1; 95% CI: 5.82–166.3, $p<0.001$) and older age (OR: 1.067; 95% CI: 1.011–1.126, $p=0.018$) were found as independent predictors for occurrence of bleeding events.

Discussion

Our study results showed that all HRQoL scores were significantly lower and HADS scores were significantly higher in the warfarin group than in the NOAC group. The annual number of hospital admissions was significantly higher in the warfarin group, which showed a negative correlation with all subscales of HRQoL questionnaire and a positive correlation with HADS-A/HADS-D scores. Warfarin-treated patients experienced more bleeding episodes, and all HRQoL scores were significantly lower and the HADS-D score was significantly higher among patients who had a bleeding episode. Also, warfarin treatment and older age conferred greater risks for bleeding.

HRQoL objects to get information about difficulties of living with a disease that are variable for each patient due to the subjective and diverse perception (14). Improvement in functional capacity or alleviation of AF-related symptoms (7) is not aimed at when using OACs in AF patients; OACs protect patients from thromboembolic complications. Chronic use of VKAs constitutes a well-defined risk without any symptomatic

Table 5. Comparison of quality of life, anxiety, depression levels and annual number of hospital admissions between warfarin and NOAC groups after adjusting for age, gender, duration of OAC therapy and drug compliance

Variables	Warfarin group (n=91)	NOAC group (n=91)	<i>p</i> [†]
Physical functioning	58.8 (52.5–65.0)	68.4 (60.9–75.8)	0.100
Role physical	45.6 (36.3–54.9)	73.8 (62.8–84.8)	<0.001
Bodily pain	57.2 (49.4–65.0)	77.1 (67.9–86.4)	0.006
General health	40.0 (33.5–46.5)	55.4 (47.7–63.1)	0.011
Vitality	44.1 (38.1–50.2)	57.4 (50.2–64.6)	0.019
Social functioning	53.9 (48.0–59.9)	82.2 (75.2–89.2)	<0.001
Role emotional	45.7 (38.1–53.3)	78.0 (69.0–87.0)	<0.001
Mental functioning	60.3 (55.7–64.9)	70.4 (65.0–75.9)	0.019
HADS-A	6.2 (5.8–6.6)	4.6 (4.2–5.1)	<0.001
HADS-D	4.9 (4.5–5.3)	3.6 (3.1–4.1)	<0.001
Annual number of hospital admissions	12.8 (11.9–13.7)	4.9 (3.8–6.0)	<0.001

[†]Analysis of covariance (ANCOVA); data were given as mean (95% confidence interval) after adjusting for age, gender, duration of oral anticoagulant therapy and drug compliance; HADS - Hospital Anxiety and Depression Scale; HADS-A - Anxiety subscale of HADS; HADS-D - Depression subscale of HADS

benefit that results in lifestyle changes and influences HRQoL (15). Before the development of NOACs, VKAs were widely used for the prophylaxis of thromboembolic events; however, requirement for strict blood monitoring has a negative impact on HRQoL in such patients (14). Therapy with VKAs is complicated because of their variable biological effects, necessity for dietary restrictions, narrow therapeutic index and adverse events such as thrombotic and bleeding events (5, 14).

Several studies have investigated the effect of OAC therapy on HRQoL (16). Corbi et al. (15) found worse scores of HRQoL among women, elderly, those with less than 1 year of therapy and those with an indication other than metallic prosthetic heart valve for OAC use. In their study group, warfarin was the most prescribed OAC (83.1%). They suggested that patients with longer use of OAC (>10 years) had enough time to adapt to the therapy. In our study, the median duration of OAC therapy was 20 months in the warfarin group and 9 months in the NOAC group. When compared with the previous study, the anticoagulation time was relatively shorter in our study cohort. Although we observed a longer duration of therapy in the warfarin group when compared with the NOAC group, we observed worse HRQoL scores among warfarin users. Somehow NOAC-treated patients mostly had better EHRA scores that may lead to better HRQoL scores. We thought that due to the limited clinical experience with NOACs, clinicians might prefer to use NOACs among relatively more healthy subjects because they may experience lesser side effects or when they face them, they may recover easily. Lancaster et al. (17) observed no significant difference between warfarin-treated and control patients regarding HRQoL until a bleeding episode had occurred. They concluded that patients with bleeding episode had a significant decrease in perceived health. We observed higher minor bleeding events in the warfarin group and worse HRQoL scores were noted in the warfarin group. Although in the warfarin group, the duration of therapy was longer

than that in the NOAC group, after adjustment according to the duration of OAC therapy, usage of warfarin was still an independent predictor of bleeding events. In a study conducted by Alegret et al. (18), they observed worse HRQoL related to some aspects among VKA-treated patients as compared with NOAC-treated patients. However, the difference between the two groups disappeared after 6 months of therapy. Moreover, Monz et al. (19) failed to show any difference in HRQoL measures between warfarin and dabigatran-treated patients despite the known complexities of warfarin treatment. In the Turkish population, less than half of the patients (41.3%) who were on OAC treatment had effective INR levels and 11% of them had labile INR value (1), which may directly worsen warfarin-treated patients' HRQoL. Therefore, we observed that warfarin-treated patients had worse HRQoL scores than NOAC-treated patients beyond the 6 months of therapy (20 vs. 9 months).

HADS is a reliable and valid instrument to assess depression and anxiety in patients and in the general population (20). We observed a positive correlation between HADS scores and the annual number of hospital admissions, which means that the warfarin group was more prone to anxiety and depression. In our study, 37.3% patients had INR levels between 2.0 and 3.0, which is consistent with the results of the AFTER study (41.3%) (1). When we analysed patients according to having effective INR levels, higher HADS scores were observed among patients with ineffective INR levels. We think that difficulties of gaining an effective INR level may have an important influence on patients' emotional status. In a previous study, treatment with NOACs revealed better HADS scores among elderly AF patients and treatment with NOACs was psychologically well accepted than warfarin therapy (21). We can conclude that NOACs may have positive effects on anxiety and depression symptoms in non-valvular AF patients.

Social desirability, described as the tendency to answer questions in a socially accepted manner for preserving self-image or

avoiding negative consequences (22), may be another reason for better HRQoL assessment and better HADS scores in the NOAC group. All patients in the NOAC group had previously switched from warfarin to NOAC therapy due to labile INRs or complications; this may have led them to report better results with the new medication to represent a favourable image. In addition to the lack of frequent laboratory follow-up with NOACs, being treated with a more expensive drug may improve patients' perception of HRQoL (23).

Study limitations

This study has several limitations. First, this was a cross-sectional study with a relatively small sample size. Second, it was a single-centre study. Third, in the NOAC group, we did not classify the patients according to the type of NOACs; instead, all patients were evaluated together. Fourth, in the NOAC group, we included only those patients who had previously used warfarin, which may have given them an opportunity to compare both OAC therapies; on the other hand, it may have led to a bias. Finally, the questionnaire for assessing HRQoL was not particular to our study population, but it evaluates patients' perception of their health status and both physical and functional dimensions in addition to emotional and social ones. In this context, modified questionnaires for the Turkish population may provide precise evaluation of the current issue.

Conclusion

Warfarin-treated patients had higher levels of self-reported symptoms of depression and anxiety and compromised HRQoL when compared with NOAC-treated patients. The results may be explained by the higher rates of bleeding episodes and higher number of hospital admissions, which may cause restrictions in life while on warfarin treatment.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - K.G.B., M.M.B.; Design - K.G.B., M.M.B., O.M., M.T.S., H.S., U. C.; Supervision - O.M., M.T.S., H.S.; Resource - M.S., S.K., K.G.B., M.K.A.; Data collection &/or processing - U.C., F.Ş., K.G.B., M.K.A., M.S., S.K.; Analysis &/or interpretation - M.M.B., M.S., S.K., O.M., F.Ş., K.G.B., M.K.A.; Literature search - M.M.B., O.M., F.Ş., K.G.B., M.K.A., U.C., M.S., S.K.; Writing - K.G.B., M.M.B., O.M., M.T.S., H.S.; Critical review - O.M., M.T.S., H.S., U.C.

References

1. Ertaş F, Kaya H, Yüksel M, Soyduñç MS, Alan S, Ülgen MS. Atrial Fibrillation in Turkey: Epidemiologic Registry (AFTER) study design. *Anatol J Cardiol* 2013; 13: 339-43. [\[Crossref\]](#)
2. 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). *European Heart Rhythm Association; European Association for Cardio-Thoracic Surgery. Europace* 2010; 12: 1360-420.
3. Camm AJ, Lip GY, De Caterina R, Savelieva I, Atar D, Hohnloser SH, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation-developed with the special contribution of the European Heart Rhythm Association. *Europace* 2012; 14: 1385-413. [\[Crossref\]](#)
4. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol* 2014; 64: e1-76. [\[Crossref\]](#)
5. Kepez A, Erdoğan O. Anticoagulation for non-valvular atrial fibrillation: new anticoagulant agents. *Anatol J Cardiol* 2013; 13: 379-84.
6. Ansell J, Hirsh J, Poller L, Bussey H, Jacobson A, Hylek E. The pharmacology and management of the vitamin K antagonists: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; 126: 204S-33S. [\[Crossref\]](#)
7. Casais P, Meschengieser SS, Sanchez-Luceros A, Lazzari MA. Patients' perceptions regarding oral anticoagulation therapy and its effect on quality of life. *Curr Med Res Opin* 2005; 21: 1085-90.
8. Mani H, Lindhoff-Last E. New oral anticoagulants in patients with nonvalvular atrial fibrillation: a review of pharmacokinetics, safety, efficacy, quality of life, and cost effectiveness. *Drug Des Devel Ther* 2014; 8: 789-98. [\[Crossref\]](#)
9. Avila CW, Aliti GB, Feijó MK, Rabelo ER. Pharmacological adherence to oral anticoagulant and factors that influence the international normalized ratio stability. *Rev Lat Am Enfermagem* 2011; 19: 18-25.
10. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; 30: 473-83. [\[Crossref\]](#)
11. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67: 361-70. [\[Crossref\]](#)
12. Tamam MO, Bağcıođlu E, Mülazımođlu M, Tamam L, Özpaccacı T. Evaluation of anxiety and depression in patients prior to myocardial perfusion scintigraphy. *Int J Psychiatry Clin Pract* 2012; 16: 93-7.
13. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986; 24: 67-74. [\[Crossref\]](#)
14. Prins MH, Marrel A, Carita P, Anderson D, Bousser MG, Crijs H, et al. Multinational development of a questionnaire assessing patient satisfaction with anticoagulant treatment: the "Perception of Anticoagulant Treatment Questionnaire" (PACT-Q). *Health Qual Life Outcomes* 2009; 7: 9. [\[Crossref\]](#)
15. Corbi IS, Dantas RA, Pelegrino FM, Carvalho AR. Health related quality of life of patients undergoing oral anticoagulation therapy. *Rev Lat Am Enfermagem* 2011; 19: 865-73. [\[Crossref\]](#)
16. Ynsaurriaga FA, Peinado RP, Ormaetxe Merodio JM. Atrial fibrillation and quality of life related to disease and treatment: focus on anticoagulation. *Future Cardiol* 2014; 10: 381-93. [\[Crossref\]](#)
17. Lancaster TR, Singer DE, Sheehan MA, Oertel LB, Maraventano SW, Hughes RA, et al. The impact of long-term warfarin therapy on quality of life. Evidence from a randomized trial. *Boston Area Anticoagulation Trial for Atrial Fibrillation Investigator. Arch Intern Med* 1991; 151: 1944-9. [\[Crossref\]](#)

18. Alegret JM, Viñolas X, Arias MA, Martínez-Rubio A, Rebollo P, Ràfols C, et al. New oral anticoagulants vs. vitamin K antagonists: benefits for health-related quality of life in patients with atrial fibrillation. *Int J Med Sci* 2014; 11: 680-4. [\[Crossref\]](#)
19. Monz BU, Connolly SJ, Korhonen M, Noack H, Pooley J. Assessing the impact of dabigatran and warfarin on health-related quality of life: results from an RE-LY sub-study. *Int J Cardiol* 2013; 168: 2540-7.
20. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the hospital anxiety and depression scale. An updated literature review. *J Psychosom Res* 2002; 52: 69-77. [\[Crossref\]](#)
21. Fumagalli S, Cardini F, Roberts AT, Boni S, Gabbai D, Calvani S, et al. Psychological effects of treatment with new oral anticoagulants in elderly patients with atrial fibrillation: a preliminary report. *Aging Clin Exp Res* 2015; 27: 99-102. [\[Crossref\]](#)
22. Gagné C, Godin G. Improving self-report measures of non-adherence to HIV medications. *Psychol Health* 2005; 20: 803-16. [\[Crossref\]](#)
23. Espay AJ, Norris MM, Eliassen JC, Dwivedi A, Smith MS, Banks C, et al. Placebo effect of medication cost in Parkinson disease: A randomized double-blind study. *Neurology* 2015; 84: 794-802.