European Journal of Therapeutics

DOI: 10.5152/EurJTher.2018.602

Original Research

Effects of Regular Follow-up on Quality of Life and Warfarin Efficiency in Rural Patients

Salih Kılıç[1], Erhan Saraçoğlu[1], Yusuf Çekici[1], Dilara Deniz Kılıç[2], Arafat Yıldırım[1], Zülfiye Kuzu[1]

[1]Clinic of Cardiology, Dr. Ersin Arslan Training and Research Hospital, Gaziantep, Turkey

[2]Clinic of Internal Medicine, Nizip State Hospital, Gaziantep, Turkey

ABSTRACT

Objective: This study aims to evaluate the effects of regular follow-up and education on warfarin efficiency, satisfaction, and the quality of life in patients from rural areas.

Methods: A total of 133 patients from rural areas taking warfarin were followed up for the mean of 17.4±0.5 months (mean age 58±13 years, 72.9% female). All patients were educated and followed up by a single cardiologist prospectively. A list and an illustrated booklet presenting foods that interact with warfarin and a follow-up chart were prepared for each patient. An illustrated scheme of pills that were to be taken every day was prepared for illiterate patients. The international normalized ratio (INR) values during and 1 year before the study were recorded from the hospital system, and the time in therapeutic range (TTR) was calculated. The Duke Anticoagulation Satisfaction Scale was conducted at the start and end of the study to determine patients' satisfaction with warfarin use. Furthermore, the Medical Outcomes Study Form 36 (SF-36) was used for determining the health-related quality of life (HRQoL).

Results: A total of 45.9% of patients were illiterate, and 33.8% were primary school graduates. The median TTR during the follow-up increased significantly compared with the previous year [40.0 (IQR 36.5) vs. 62.1 (IQR 29.3); p<0.001]. Furthermore, the number of patients with TTR>70% increased significantly (36.8% vs. 21.1%, respectively; p<0.001). Unfortunately, patients' HRQoL and satisfaction with warfarin use were found to have deteriorated significantly compared to the basal levels.

Conclusion: We found that the efficiency of warfarin increased significantly, but interestingly, HRQoL and the satisfaction with warfarin use deteriorated significantly after regular education and follow-up in patients from rural areas.

Keywords: Duke Anticoagulation Satisfaction Scale, health-related quality of life, warfarin therapy

INTRODUCTION

Warfarin is an efficient oral anticoagulant used to prevent thromboembolic events in patients with atrial fibrillation (AF) or a mechanical heart valve (MHV). The efficacy and safety of warfarin strongly depend on the anticoagulation intensity measured in terms of the international normalized ratio (INR). For achieving a high-quality, safe, and minimally complicated treatment, the time in therapeutic range (TTR) is targeted at >70 (1). Many studies have shown that TTR levels differ greatly from the desired levels in the Turkish population (2-4). Çelik et al. (4) showed that only 55% of patients taking warfarin were aware of food–drug interactions. Other studies reported that the elderly and patients with a lower education level were likelier to have lower awareness of warfarin treatment, possibly because they faced difficulties in understanding educational materials and communicating with healthcare providers (5). Therefore, the educational materials and their content, duration, and frequency of education should be selected according to the target patient population. Frequent INR controls, long waits at hospitals, dietary limitations, and bleeding-related concerns reduce the health-related quality of life (HRQoL) of patients taking warfarin (6). Two basic approaches are used for measuring the HRQoL of patients receiving anticoagulants: generic and condition specific. Ideally, both approaches should be used for evaluating patients' quality of life (7).

This study aimed to evaluate the effects of a regular follow-up and education on warfarin efficiency, satisfaction, and the quality of life in patients from rural areas.

METHODS

This prospective, observational study was performed in a secondary-level hospital in a rural region of Turkey (Nizip State Hospital, Gaziantep) from January 2016 to June 2017. It was approved by the Gaziantep University ethical committee (30.05.2016/180), following which recruitment started in January 2016. All patients

How to cite: Kılıç S, Saraçoğlu E, Çekici Y, Kılıç DD, Yıldırım A, Kuzu Z. Effects of Regular Follow-up on Quality of Life and Warfarin Efficiency in Rural Patients. Eur J Ther 2019; 25(3): 183-8.

ORCID IDs of the authors: S.K. 0000-0002-3579-3747; E.S. 0000-0003-3797-521X; Y.Ç 0000-0002-4585-3707; D.D.K. 0000-0002-3699-2158; A.Y. 0000-0002-2798-7488; Z.K. 0000-0001-5378-5516

Corresponding Author: Salih Kılıç **E-mail:** kilicsalihhh@gmail.com

Received: 10.04.2018 • **Accepted:** 11.06.2018 • **Available Online Date:** 22.03.2019

who gave their verbal or written consent to participate in the study were recruited. All patients were educated and followed up by a single cardiologist during the study. Patients who agreed to participate and were recruited had been taking warfarin for any reason for at least 1 year and were regularly followed up in the same hospital (n=137). The inclusion criteria were age ≥18 years, volunteering to participate in the study, and being followed up at the same hospital for at least 1 year. The single exclusion criterion was the gap of more than 59 days between two prospective follow-ups. Hypertension (HT) was defined as repeated blood pressure measurement >140/90 mmHg or chronic treatment with antihypertensive medications. Diabetes mellitus (DM) was defined as a previous diagnosis and/or fasting blood glucose >126 mg/dL or the use of antidiabetic medications. Hyperlipidemia was defined as low-density lipoprotein cholesterol (LDL-C) >200 mg/dL or the use of lipid-lowering medications (8). Cigarette smoking was defined as smoking ≥1 cigarette a day for at least 1 year without any attempts at quitting. Ischemic heart disease was defined as having previous percutaneous transluminal coronary angioplasty and/or stenting, coronary bypass grafting, or stable coronary artery disease. All patients were informed in detail on initial visit about why they were taking warfarin, how they would take it, how doses would be adjusted, and what the frequency of follow-up visits was. All patients were also informed about food–drug interactions. A list of frequently consumed local foods that interacted with warfarin was given to all patients, and a booklet with pictures of these foods was provided to illiterate patients. A follow-up chart was prepared for all patients, and the daily number of warfarin pills, INR values, and next visit details were recorded. For illiterate patients, the daily numbers of warfarin pills were illustrated for each day of the week. The therapeutic range in patients with warfarin for AF or aortic valve replacement was considered as the INR levels of 2.0–3.0. For patients with the mitral valve or two-valve (mitral and aortic) replacement, the INR levels were considered as 2.5–3.5. All INR levels during the study and 1-year period prior to the study were recorded from the hospital laboratory database, and the TTR was calculated using Rosendaal's algorithm (9). The annual INR after the follow-up was calculated as (all INR levels in follow-up × 12)/(duration of study in months). All adverse events during the study period were recorded. Ischemic stroke was defined as neurologist-confirmed symptomatic ischemic cerebral infarction with an apparent brain lesion in imaging studies. Transient ischemic attack was defined as a neurologist-confirmed transient episode of neurologic dysfunction without a brain lesion in imaging studies. Major bleeding was defined as symptomatic bleeding in a critical organ, transfusion of two or more units of blood, or decrease in the hemoglobin level of at least 2 g/L. All other bleeding was defined as minor bleeding.

Questionnaires

Two questionnaires were administered to all patients to evaluate their HRQoL and satisfaction with warfarin use at the start and end of the study. The Duke Anticoagulation Satisfaction Scale (DASS) questionnaire was used to assess the satisfaction with warfarin use (10). Furthermore, the Medical Outcomes Study Form 36 (SF-36) questionnaire was used to assess HRQoL (11). The validity and reliability of the Turkish versions of both scales have been reported previously (12, 13). SF-36 comprises eight subscales that reflect both physical health (physical functioning, role-physical, bodily pain, and general health) and mental health (vitality, social functioning, role emotional, and mental functioning). The scores range from 0 to 100, where higher scores indicate better functions (11). The DASS scale includes 25 questions. The pattern of the questions is arranged to roughly correspond to three possible dimensions pertaining to anticoagulation: limitations (e.g., fear of bleeding, dietary restrictions); displeasure and burden (regular return to medical visit and wait for blood test results), and positive psychological impact. Patients respond to these questions on a 7-point Likert scale. Lower scores indicate higher satisfaction. The overall score varies from 25 to 175. The instrument is divided in three domains: limitations (score from 9 to 63), displeasure and burden (score from 8 to 56), and psychological impact (score from 8 to 56). The subscales were analyzed by adding the answers to the items (varying from 1 to 7 for each item) in each domain, and the total score was obtained by adding up all questionnaire items.

Statistical Analysis

The variables were investigated using the Kolmogorov–Smirnov test to determine whether they were normally distributed. The mean and standard deviations of normally distributed variables and the IQR of non-normally distributed variables were calculated. The TTR values and questionnaire results (DASS and SF-36) computed at the start and end of the study were compared using the paired sample t-test and Wilcoxon test. The proportions of patients with TTR values >70% at the start and end of the study were presented as a percentage, and the change was compared using the McNemar test. A p-value <0.05 was considered to indicate a statistically significant result. All data were analyzed using the Statistical Package for the Social Sciences Version 22.0 (SPSS IBM Corp.; Armonk, NY, USA) software for Windows.

RESULTS

A total of 137 patients were recruited for the study. Four patients with irregular follow-up were excluded; the remaining 133 patients (72.9% female, mean age 58.1±12 years) were followed up for a mean of 17.4±0.5 months. Table 1 summarizes the demographic characteristics of patients. The primary indication of warfarin use was MHV and AF (72.9% and 27.1%, respectively). The majority of the study population was either illiterate or had graduated from primary school (45.9% and 33.8%, respectively). The median duration for which patients had been taking warfarin was 7.0 (IQR 6) years, and 60.2% of patients had been taking warfarin for >5 years. The most frequent comorbidities were HT, heart failure, ischemic heart disease, and DM. Approximately 22.5% (n=30) of patients had a previous history of bleeding (40% [n=12] had history of major bleeding), and 9.0% (n=12) of patients had a history of ischemic events (8 and 4 had history of transient ischemic attack and ischemic stroke, respectively). The median TTR levels during the follow-up increased significantly compared with those in the previous year (40.0 [IQR 36.5] vs. 62.1 [IQR 29.3]; p <0.001] (Figure 1). Moreover, the ratio of patients with TTR levels ≥70% increased significantly (21.1% vs. 36.8%; p<0.001) at the end of the study (Table 2). The basal demographic and clinical characteristics of patients who with

Table 1. Basal Demographic and Clinical Characteristics of Study Population

Parameters	Values	TTR≥70% (n=49)	TTR<70% (n=84)	p
Age years, mean±SD	58.1±12.8	57.3±13.3	58.4±12.7	0.630
Female n, (%)	97 (72.9)	31 (63.3)	66 (78.6)	0.550
BMI (kg/m^2)	28.7±4.6	29.1±4.6	28.3±4.6	0.330
Time of warfarin use years, median (IQR)	7.0 (6)	5.0 (6.5)	8.0 (5.0)	0.032
Hypertension n, (%)	55 (41.4)	19 (38.8)	36 (42.9)	0.645
Diabetes mellitus n, (%)	32 (24.1)	13 (26.5)	19 (22.6)	0.611
Heart failure n, (%)	45 (33.8)	15 (30.6)	30 (35.7)	0.549
Cerebrovascular events n, (%)	12 (9.0)	2 (4.1)	10 (11.9)	0.129
Ischemic heart disease n, (%)	31 (23.3)	14 (28.6)	17 (20.2)	0.273
Smoke n, (%)	10 (7.5)	2 (4.1)	8 (9.5)	0.251
Chronic kidney disease n, (%)	12 (9)	4 (8.2)	8 (9.5)	0.792
All bleeding n, (%)	30 (22.5)	6 (12.2)	24 (28.6)	0.030
Major bleeding n, (%)	12 (9.0)	2 (4.1)	10 (11.9)	0.129
Non steroid anti-inflammatory drug use n, (%)	82 (61.7)	30 (61.2)	52 (61.9)	0.724
Antiplatelet use n, %	12 (9)	3 (6.1)	9 (10.7)	0.373
Education				
Illiterate n, (%)	61 (45.9)	20 (40.8)	41 (48.8)	
Primary school n, (%)	45 (33.8)	17 (34.7)	28 (33.3)	0.139
High school n, (%)	19 (14.3)	6 (12.2)	13 (15.5)	
University n, (%)	8 (6)	2 (4.1)	6 (7.1)	

BMI: body mass index; IQR: interquartile range; SD: standard deviation; TTR: time in therapeutic range

Table 2. Comparison of Time in Therapeutic Range Pre- and Post-study

Parameters	Pre-study	Post-study	p¶
TTR %, median (IQR)	40 (36.5)	62.1 (29.3)	<0.001
TTR ≥70% n,%	28 (21.1)	49 (36.6)	0.001*
Annual number of INR, median (IQR)	8.5 (4.2)	12 (2.6)	<0.001

INR: international normalized ratio; IQR: interquartile range; TTR: time in therapeutic range
¶ Wilcoxon test; *McNemar test

TTR≥70% and TTR<70% at the end of the study are summarized at Table 1. There were no significant differences between the two groups, expect the median time of warfarin use and history of all bleedings. The ratio of all bleeding was significantly higher in patients with TTR<70, and median time of warfarin use was significantly higher in patients with TTR≥70%. The median annual INR in the follow-up also increased significantly (11.7±2.8 vs. 8.8±4.0; p<0.001). During the follow-up, 17 (12.8%) patients suffered bleeding events (5 suffered major bleeding), 2 patients had transient ischemic attack, and 1 had ischemic stroke. No deaths occurred during the follow-up. Table 3 shows the difference between the DASS scores at the start and end of the study. The median of the DASS score and its subscales that were evaluated separately increased significantly at the end of the study (p<0.001 for all). Similarly, the role physical, physical functioning, mental functioning, bodily pain, general health, social functioning, vitality, and role emotional scores of the SF-36 scale decreased significantly at the end of the study (p<0.001 for all) (Table 3). Moreover, there were no significant differences between patients with TTR≥70 and TTR<70 in terms of both the DASS score and SF-36 subscales.

DISCUSSION

The present study provided two major results. First, the TTR level of patients from rural areas who were uneducated or had a low education level were significantly low; however, they improved dramatically after regular education with appropriate materials and follow-up. Second, patients' satisfaction with warfarin use and HRQoL unfortunately worsened significantly after regular education and follow-up.

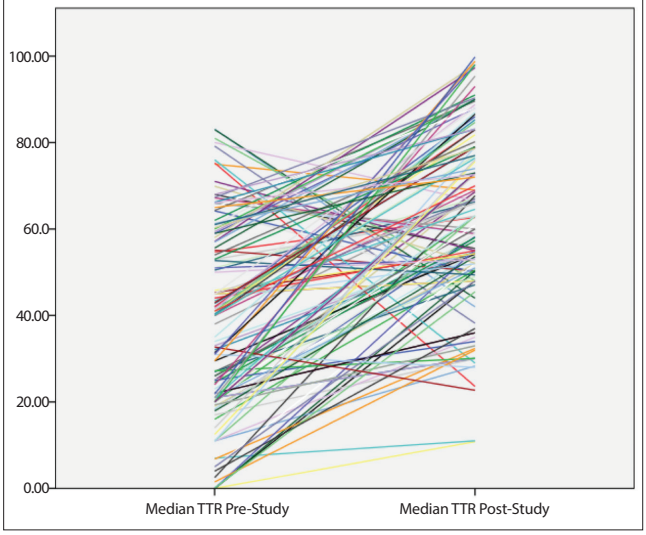
Previous studies showed that the mean TTR level was low in the Turkish population. In the AFTER study (epidemiology of AF in Turkey), only 41.3% of patients showed efficient INR levels (3). Turk et al. (2) conducted a multicenter prospective study and found that the mean TTR level was 42.3±18%. Similarly, the WARFARIN-TR (Awareness, Efficacy, Safety, and Time in Therapeutic Range of Warfarin in the Turkish population) study reported

Table 3. Comparison of Duke Anticoagulation Satisfaction Scale and Medical Outcomes Study Form 36 Pre–and Post–study and Between TTR≥70% and TTR<70%

Parameters	Pre–study Median (IQR)	Post–study Median (IQR)	p*	TTR≥70% (n=49)	TTR<70% (n=84)	p
DASS						
Total, mean±SD	82.7±18.1	135.2±15.6	<0.001¶	135.4±8.5	137.1±11.1	0.349
Limitations	31 (48)	52 (21)	<0.001	52.5±4.3	52.2±4.4	0.557
Displeasure and burden	30 (47)	49 (45)	<0.001	48.8±3.9	49.6±7.1	0.464
Positive psychological impact	24 (22)	35 (18)	<0.001	34.5±3.2	34.9±3.4	0.451
SF–36						
Role physical	32 (26)	26 (23)	<0.001	25 (30)	26 (30)	0.771
Physical functioning	65 (30)	50 (30)	<0.001	54 (22)	48 (16)	0.080
Bodily pain	67.5 (54)	57.5 (35)	<0.001	55 (42)	60 (40)	0.177
General health	35 (25)	25 (50)	<0.001	25 (50)	25 (80)	0.158
Social functioning	62.5 (50)	50 (50)	<0.001	50 (37.5)	50 (25)	0.721
Vitality	45 (35)	35 (25)	<0.001	37.5 (20)	35 (25)	0.585
Role emotional	35.1 (33)	20 (33)	<0.001	20 (30)	20 (25)	0.897
Mental functioning	58 (49)	44 (35)	<0.001	46 (25)	43 (30)	0.786

DASS: Comparison of Duke Anticoagulation Satisfaction Scale; IQR: interquartile range; SD: standard deviation; SF–36: Medical Outcomes Study Form 36
¶ Paired samples t–test; * Wilcoxon test

Figure 1. Pre- and Post-study Median Level of Time in Therapeutic Range (TTR) for Each Participant



that the 1-year average TTR level was 49.5±22.9% (4). Furthermore, a subgroup analysis of the WARFARIN-TR study showed that themean TTR levels differed significantly across different geographical regions of Turkey (14). In this analysis, the mean TTR level in the Southeastern Anatolia region was found to be 44.3±23.5%; this was significantly lower than the mean for Turkey. Similarly, our study in the Southeastern Anatolia region of Turkey reported low TTR levels (38.7±22.03) for patients in the period before the study. However, after regular education and follow-up, patients' TTR levels improved significantly. Moreover, the number patients with TTR ≥70 increased significantly. The INR monitoring can be performed in hospitals, general outpatient clinics, and specialized INR outpatient clinics, as well as through self-monitoring (15-18). The highest TTR can be achieved through self-monitoring; however, the most significant limitations in this regard are the patient's compatibility, ability to use necessary medical devices, and awareness of required drug dose to be set (17, 19). Self-monitoring was not applicable for our patients because most of them were illiterate or were at most primary school graduates. However, we showed that the TTR level could be improved significantly through a regular follow-up at, for example, specialized INR outpatient clinics. The main difficulties faced in warfarin use are frequent food–drug interactions and the need for lifetime use. Moreover, frequent hospital visits, long waits at hospitals, and bleeding-related worries are among the primary difficulties faced in warfarin use that affect patients' quality of life and satisfaction (20-22). Although there are methodological differences between studies, long-term warfarin use was found to have significant and negative effects on the quality of life (23, 24). Previous studies revealed that the mean DASS scores were different among populations (7, 25). The mean of the scale for the Turkish population (85.0±25.1) was found to be higher than those of the original scale scores (55.0±17.6) and the scores determined in the Brazilian–Portugal validation (57.9±16.5) (7, 12, 25). This result shows that the treatment satisfaction of Turkish patients is lower than that of other populations, and they perceive more problems. Our results show that although the mean DASS (82.1±18.1) of patients before the study was similar to that of Turkish population, it unfortunately increased at the end of the study. Meanwhile, the SF-36 subscale scores decreased. These re-

sults show that, unexpectedly, patients' satisfaction with warfarin use and their health-related quality of life deteriorated after regular follow-up and education. This can be attributed to factors like a regular follow-up, development of awareness about the effect mechanism and adverse events related to warfarin use, dietary limitations, worries about drug interactions, and more frequent hospital visits. Shifting from a solitary and snugger (without being careful about the diet or going for follow-up visits by their own choice) follow-up pattern to a more regular and systematic follow-up design that also includes the participation of the physician might have negatively affected their quality of life. In addition, although warfarin protects patients from serious complications such as thromboembolism, it does not provide a symptomatic improvement, and it also imposes additional burdens such as bleeding risk, dietary limitations, drug interaction, and regular follow-up; these factors may explain the decreases in the patients' quality of life (26). New-generation oral anticoagulants that can be applied as alternatives for patients taking warfarin for nonvalvular atrial fibrillation have come into use recently. These drugs have similar efficacy to previous ones and afford significant advantages such as not requiring a close follow-up, the absence of food–drug interactions, and causing less bleeding (27-30). New-generation oral anticoagulants can be preferred to warfarin in patients who have a low TTR level or are dissatisfaction after a regular follow-up. Moreover, for patients who use warfarin due to MHV, appropriate interventions should be done considering the special conditions of the patients.

The main limitations of our study are its single-center design, a low number of patients, and short follow-up. In addition, the pre-study INR measurements were obtained from hospital records, and we cannot exclude the possibility of other measurements at another facility. Another limitation is that because most patients were uneducated or had a low education level, they may have responded incorrectly to the questionnaires.

CONCLUSION

The present study showed that an appropriate educational material and follow-up can significantly increase the TTR levels of patients from rural areas who are mostly illiterate or primary school graduates. However, only one-third of patients had TTR levels >70%, suggesting that different approaches should be used to increase the efficiency of warfarin use. Finally, deteriorations in HRQoL can be explained by the increased awareness and additional burden that comes with a regular follow-up.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Gaziantep University (30.05.2016/180).

Informed Consent: Written and verbal informed consent was obtained from patients and patients' parents who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – S.K.; Design – S.K.; Supervision – E.S.; Resources – S.K.; Materials – S.K., E.S., Y.Ç., D.D.K., A.Y., Z.K.; Data Collection and/or Processing – A.Y., Y.Ç.; Analysis and/or Interpretation – D.D.K.; Literature Search – S.K.; Writing Manuscript – S.K., E.S.; Critical Review – E.S.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. 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. Eur Heart J 2012; 33: 2719-47. [CrossRef]
2. Turk UO, Tuncer E, Alioglu E, Yuksel K, Pekel N, Ozpelit E, et al. Evaluation of the impact of warfarin time in therapeutic range on outcomes of patients with atrial fibrillation in Turkey: Perspectives from the observational, prospective WATER Registry. Cardiol J 2015; 22: 567-75. [CrossRef]
3. Ertaş F, Kaya H, Kaya Z, Bulur S, Köse N, Gül M, et al. Epidemiology of atrial fibrillation in Turkey: preliminary results of the multicenter AFTER study. Turk Kardiyol Dern Ars 2013; 41: 99-104. [CrossRef]
4. Çelik A, İzci S, Kobat MA, Ateş AH, Çakmak A, Çakıllı Y, et al. The awareness, efficacy, safety, and time in therapeutic range of warfarin in the Turkish population: WARFARIN-TR. Anatol J Cardiol 2016;16:595-600. [CrossRef]
5. Tang EO, Lai CS, Lee KK, Wong RS, Cheng G, Chan TY. Relationship between patients' warfarin knowledge and anticoagulation control. Ann Pharmacother 2003; 37: 34-9. [CrossRef]
6. Casais P, Meschengieser S, Sanchez-Luceros A, Lazzari M. Patients' perceptions regarding oral anticoagulation therapy and its effect on quality of life. Curr Med Res Opin 2005; 21: 1085-90. [CrossRef]
7. Samsa G, Matchar DB, Dolor RJ, Wiklund I, Hedner E, Wygant G, et al. A new instrument for measuring anticoagulation-related quality of life: development and preliminary validation. Health Qual Life Outcomes 2004; 2: 22. [CrossRef]
8. Tokgözoğlu L, Oğuz A, Balcı MK, Temizhan A, Altunoğlu EG, Bektaş O, et al. Turkish assessment of SURF (SUrvey of Risk Factor Management) study: Control rates of cardiovascular risk factors derived from databases of 15 different levels of health centers in Turkey. Turk Kardiyol Dern Ars 2017; 45: 398-407.
9. Rosendaal F, Cannegieter S, van der Meer F, Briët E. A method to determine the optimal intensity of oral anticoagulant therapy. Thromb Haemost 1993;69:236-9. [CrossRef]
10. Samsa G, Matchar DB, Dolor RJ, Wiklund I, Hedner E, Wygant G, et al. A new instrument for measuring anticoagulation-related quality of life: development and preliminary validation. Health Qual Life Outcomes 2004; 2: 22. [CrossRef]
11. Stewart AL, Hays RD, Ware JE Jr. The MOS short-form general health survey: reliability and validity in a patient population. Med Care 1988; 26: 724-35. [CrossRef]
12. Yıldırım JG, Temel AB. Duke antikoagülan memnuniyet ölçeğinin Türkçe formunun geçerlik ve güvenirliği. Turk Gogus Kalp Dama 2014; 22: 761-72. [CrossRef]
13. Koçyiğit H, Aydemir Ö, Fişek G, Ölmez N, Memiş A. Kısa Form-36 (KF-36)'nın Türkçe versiyonunun güvenilirliği ve geçerliliği. İlaç Tedavi Derg 1999; 12: 102-6.
14. Kılıç S, Çelik A, Çakmak HA, Afşin A, Tekkeşin Aİ, Açıksarı G, et al. The time in therapeutic range and bleeding complications of warfarin in different geographic regions of Turkey: a subgroup analysis of WARFARIN-TR Study. Balkan Med J 2017; 34: 349-55. [CrossRef]
15. Connock M, Stevens C, Fry-Smith A, Jowett S, Fitzmaurice D, Moore D, et al. Clinical effectiveness and cost-effectiveness of different models of managing long-term oral anticoagulation therapy: a systematic review and economic modelling. Health Technol Assess 2007; 11: ix-66. [CrossRef]

16. Heneghan C, Alonso-Coello P, Garcia-Alamino J, Perera R, Meats E, Glasziou P. Self-monitoring of oral anticoagulation: a systematic review and meta-analysis. Lancet 2006; 367: 404-11. [CrossRef]
17. Garcia-Alamino JM, Ward AM, Alonso-Coello P, Perera R, Bankhead C, Fitzmaurice D, et al. Self-monitoring and self-management of oral anticoagulation. Sao Paulo Med J 2010; 128: 246. [CrossRef]
18. Kılıç S, Soner Kemal H, Yüce Eİ, Şimşek E, Yağmur B, Memişoğlu Akgül N, et al. Comparison of Warfarin use in terms of efficacy and safety in two different polyclinics. Anatol J Cardiol 2017; 18: 328-33. [CrossRef]
19. Ansell J, Jacobson A, Levy J, Völler H, Hasenkam JM; International Self-Monitoring Association for Oral Anticoagulation. Guidelines for implementation of patient self-testing and patient self-management of oral anticoagulation. International consensus guidelines prepared by International Self-Monitoring Association for Oral Anticoagulation. Int J Cardiol 2005; 99: 37-45. [CrossRef]
20. Prins MH, Marrel A, Carita P, Anderson D, Bousser MG, Crijns 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]
21. Dantas GC, Thompson BV, Manson JA, Tracy CS, Upshur RE. Patients' perspectives on taking warfarin: qualitative study in family practice. BMC Fam Pract 2004; 5: 15. [CrossRef]
22. Carris NW, Hwang AY, Smith SM, Taylor JR, Sando K, Powell J, et al. Patient satisfaction with extended-interval warfarin monitoring. J Thromb Thrombolysis 2016; 42: 486-93. [CrossRef]
23. Kneeland PP, Fang MC. Current issues in patient adherence and persistence: focus on anticoagulants for the treatment and prevention of thromboembolism. Patient Prefer Adherence 2010; 4: 51-60. [CrossRef]
24. Das AK, Ahmed A, Corrado OJ, West RM. Quality of life of elderly people on warfarin for atrial fibrillation. Age Ageing 2009; 38: 751-4. [CrossRef]
25. Pelegrino FM, Dantas RA, Corbi IS, da Silva Carvalho AR, Schmidt A, Pazin Filho A. Cross-cultural adaptation and psychometric properties of the Brazilian-Portuguese version of the Duke Anticoagulation Satisfaction Scale. J Clin Nurs 2012; 21: 2509-17. [CrossRef]
26. 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]
27. Wallentin L, Yusuf S, Ezekowitz MD, Alings M, Flather M, Franzosi MG, et al. Efficacy and safety of dabigatran compared with warfarin at different levels of international normalised ratio control for stroke prevention in atrial fibrillation: an analysis of the RE-LY trial. Lancet 2010; 376: 975-83. [CrossRef]
28. Lopes RD, Alexander JH, Al-Khatib SM, Ansell J, Diaz R, Easton JD, et al. Apixaban for reduction in stroke and other ThromboembolIc events in atrial fibrillation (ARISTOTLE) trial: design and rationale. Am Heart J 2010; 159: 331-9. [CrossRef]
29. ROCKET AF Study Investigators. Rivaroxaban-once daily, oral, direct factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation: Rationale and Design of the ROCKET AF study. Am Heart J 2010; 159: 340-7. [CrossRef]
30. Ruff CT, Giugliano RP, Antman EM, Crugnale SE, Bocanegra T, Mercuri M, et al. Evaluation of the novel factor Xa inhibitor edoxaban compared with warfarin in patients with atrial fibrillation: Design and rationale for the Effective aNticoaGulation with factor xA next GEneration in Atrial Fibrillation–Thrombolysis In Myocardial Infarction study 48 (ENGAGE AF–TIMI 48). Am Heart J 2010; 160: 635-41. [CrossRef]