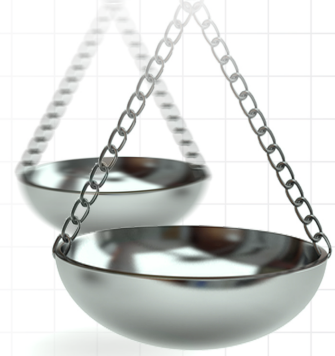
Research Article



Journal of Comparative Effectiveness Research

Satisfaction, quality of life and perception of patients regarding burdens and benefits of vitamin K antagonists compared with direct oral anticoagulants in patients with nonvalvular atrial fibrillation

Aim: To compare the satisfaction of patients treated with vitamin K antagonists (VKA) with that of patients treated with direct oral anticoagulants (DOACs) and to determine the impact on quality of life of both treatments in patients with nonvalvular atrial fibrillation (NVAF). **Methods:** Cross-sectional multicenter study in which outpatients with NVAF completed the ACTS (Anti-Clot Treatment Scale), SAT-Q (Satisfaction Questionnaire) and EQ-5D-3L (EuroQol 5 dimensions questionnaire, 3 level version) questionnaires. **Results:** The study population comprised 1337 patients, of whom 587 were taking DOACs and 750 VKAs. Compared with VKAs, DOACs were more commonly prescribed in patients with a history of stroke and in patients with a higher thromboembolic risk. The study scores were as follows: SAT-Q: 63.8 ± 17.8; EQ-5D-3L total score: 75.6 ± 20.9; visual analog scale: 63.1 ± 20.6; ACTS Burdens: 51.8 ± 8.4 and ACTS Benefits: 11.9 ± 2.4. The ACTS Burdens score and ACTS Benefits score were higher with DOACs than with VKAs (54.83 ± 6.11 vs 49.50 ± 9.15; $p < 0.001$ and 12.36 ± 2.34 vs 11.48 ± 2.46; $p < 0.001$ respectively). **Conclusion:** NVAF patients treated with oral anticoagulants had many comorbidities and a high thromboembolic risk. Satisfaction and quality of life with oral anticoagulants were high, although they were both better with DOACs than with VKAs.

First draft submitted: 3 November 2016; Accepted for publication: 13 February 2017; Published online: 29 March 2017

Keywords: ACTS • atrial fibrillation • benefit • burdens • EQ-5D-3L • oral anticoagulation • quality of life • satisfaction • SAT-Q

Mª del Mar Contreras Muruaga*[,1], José Vivancos[2], Gemma Reig[2], Ayoze González[3], Pere Cardona[4], José Mª Ramírez-Moreno[5], Joan Martí[6], Carmen Suárez Fernández[1] & on behalf of the ALADIN Study Investigators[‡]

[1]Servicio de Medicina Interna, Hospital Universitario de La Princesa, Madrid, Spain
[2]Servicio de Neurología, Hospital Universitario de La Princesa, Madrid, Spain
[3]Servicio de Neurología y Neurofisiología Clínica, Hospital San Roque Las Palmas, Las Palmas, Spain
[4]Servicio de Neurología, Hospital Universitario de Bellvitge (HUB), Barcelona, Spain
[5]Unidad de Ictus. Servicio de Neurología. Departamento de Ciencias Biomédicas. Hospital Universitario Infanta Cristina, Madrid, Spain
[6]Servicio de Neurología, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
[‡]For the full list of investigators, please see the 'Investigators' section.
*Author for correspondence: mar.contreras4@gmail.com

Atrial fibrillation (AF) is associated with a fivefold excess risk of stroke [1–4]. Except when contraindicated, chronic oral anticoagulants are the therapy of choice for reducing the risk of thromboembolic complications in most patients with AF [2,3]. Vitamin K antagonists (VKAs) have traditionally been used for this purpose. In fact, they reduce the risk of stroke effectively, with a relatively low risk of bleeding [5]. However, VKAs have many limitations, including a narrow therapeutic window, variability of response, large number of interactions with foods or other drugs and the need for coagulation monitoring, dose adjustments and dietary restrictions [6]. These limitations most likely have a direct impact on the quality of life and satisfaction of patients taking VKAs [7].

New direct oral anticoagulants (DOACs) are at least as effective as warfarin for reducing the risk of stroke and systemic embolism in patients with nonvalvular AF (NVAF), although they have a better safety profile, including a lower risk of intracranial bleeding [8]. Importantly, since DOACs have a wide therapeutic window and a predictable anticoagulant effect, no monitoring of anticoagulant activity is required, fixed doses can be prescribed and no food restrictions are necessary [6]. Therefore, DOACs may impact satisfaction and quality of life differently than VKAs [7].

Future Medicine part of fsg

Even though improving the quality of life of patients with chronic conditions should be considered a target in itself, few data are available on the impact of anticoagulation therapy on satisfaction and quality of life in patients with AF [7]. The objective of the ALADIN trial was to validate the Anti-Clot Treatment Scale (ACTS) questionnaire in outpatients with AF treated with oral anticoagulants attended in internal medicine and neurology departments in Spain [9]. The results for validation of the ACTS questionnaire were recently published. The objectives of the present study were to analyze the impact of treatment with oral anticoagulants (VKAs and DOACs) on quality of life, satisfaction and patients' perception of the burdens and benefits of anticoagulation therapy and to identify the factors associated with these variables.

Methods

ALADIN was an observational cross-sectional study of 1337 patients from 63 neurology departments and 41 internal medicine departments in Spain. The study population comprised patients aged 18 years or older who had NVAF [3], had been treated with oral anticoagulants for at least 3 months before the inclusion and had been seen at internal medicine and neurology departments in Spain. The exclusion criteria were mitral stenosis or other significant valvulopathy that required specific treatment (implantation of a prosthetic heart valve, valvuloplasty), inability to complete the specific questionnaires, hospitalization at inclusion, participation in a clinical trial involving the use of DOACs in the 6 months before inclusion and limited life expectancy. The study was approved by the Clinical Research Ethics Committee of Hospital Universitario La Princesa, Madrid, Spain. All patients signed the written informed consent document before inclusion.

Recruitment was between September 2014 and March 2015. The study involved a single visit that coincided with one of the patient's regular follow-up visits. No specific diagnostic or therapeutic intervention was performed during the study. Data were collected from the medical history and an interview with the physician and entered into a case report form. The data recorded were sociodemographic data (age, sex, weight, marital status and occupation), AF data (date of diagnosis and type of AF), comorbidities, treatments (type of oral anticoagulant, time in therapeutic range in those patients taking VKAs and concomitant drugs), Charlson comorbidity index [10], as well as the $CHADS_2$, CHA_2DS_2-VASC and HAS-BLED scores [3]. Polypathology was defined as the presence of at least two symptomatic chronic diseases with numerous decompensations that negatively impact functional capacity and require frequent medical attention [11]. To assess patients' control of the international normalized ratio (INR), the time within the therapeutic range was calculated by both the direct method (percent time with INR values within the therapeutic range) and the Rosendaal method [12]. Adequate control of INR was defined as time in the therapeutic range ≥60% according to the direct method and ≥65% according to the Rosendaal method [3]. Polymedication was defined as using five or more prescription drugs. In addition, the physician's opinion on the importance of oral anticoagulant dosing was also sought.

All patients completed the ACTS, SAT-Q (Satisfaction Questionnaire) and EQ-5D-3L (EuroQol 5 dimensions questionnaire, 3 level version) [9]. ACTS is a patient-reported measure of satisfaction with anticoagulant treatment. It includes 12 items that assess the burdens of anticoagulant treatment and three items that assess the benefits of anticoagulant treatment. Patients are required to report their experiences with anticoagulant therapy during the previous 4 weeks on a 5-point scale of intensity (from none at all [1 point] to extreme [5 points]). The ACTS Burdens total score ranges from 12 to 60 (reverse-scored: higher score indicates lesser burden [higher satisfaction] with anticoagulant treatment), and the ACTS Benefits total score ranges from 3 to 15 (direct-scored: higher score implies higher benefit [higher satisfaction] with anticoagulant treatment) [9]. The SAT-Q is a tool that analyzes patient satisfaction with medication and healthcare. It ranges from 0 to 100 points, and a higher score represents greater satisfaction with treatment [7,9,13]. The EQ-5D-3L is a standardized instrument for use as a generic measure of health-related quality of life and of health outcomes. On the visual analog scale, quality of life and health ranged from 0 to 100, with 100 representing the best health imaginable and 0 the worst health imaginable [7,9,13].

Statistical analysis

In the descriptive analysis, quantitative variables were described with measures of central tendency and dispersion (mean and standard deviation) and qualitative variables were described as absolute (n) and relative frequencies (%). The Kolmogorov–Smirnov test was used to assess the normality of the distribution. In the bivariate analysis of two means, a parametric test (*t* test) or nonparametric test (Mann–Whitney test) was applied based on the sample distribution. Depending on the sample size, percentages were compared using the chi-square test or Fisher exact test. A logistic regression analysis was performed to identify those variables associated with satisfaction, quality of life and perception of burdens and benefits of anticoagulation therapy (EQ-5D-3L). The independent variables included in

the logistic regression analysis were ACTS Burdens, ACTS Benefits, department, type of oral anticoagulant, age, sex, $CHADS_2$, CHA_2DS_2-VASC and HAS-BLED, Charlson comorbidity index, polymedication, renal function and history of stroke. To perform the logistic regression analysis, SAT-Q data were converted into a categorical variable (satisfaction: yes [percentile ≥75]/no [percentile <75]). Propensity score matching based on multivariate analysis was performed to minimize potential selection bias. Statistical significance was set at $p < 0.05$. The statistical analysis was performed using SPSS for Windows, version 17.0 (SPSS, IL, USA).

Results

The study population comprised 1337 patients, of whom 865 (64.7%) were from the department of neurology and 472 (35.3%) were from the department of internal medicine. Paroxysmal AF was reported in 26.5% of patients, persistent AF in 6.2% and permanent AF in 70.3%. As for therapy, 750 patients (56.1%) were taking VKAs (91.9% acenocoumarol and 8.1% warfarin), and 587 patients (43.9%) were taking DOACs (42.6% rivaroxaban, 29.5% apixaban and 27.9% dabigatran). Mean time on anticoagulant therapy was 36.7 ± 48.5 months (52.28 months with VKAs and 17.07 months with DOACs). The total number of daily pills was 9.1 ± 4.5.

Analysis of the clinical characteristics of the study population according to the type of oral anticoagulant (DOACs vs VKAs) revealed that hypertension and history of stroke were more common in patients receiving DOACs than in those taking VKAs (Table 1). Similarly, the estimated glomerular filtration rate, mean $CHADS_2$ score, CHA_2DS_2-VASC score and Charlson comorbidity index were higher in patients taking DOACs. In contrast, heart failure and chronic obstructive pulmonary disease were more common in patients taking VKAs.

Among patients taking VKAs, 8.1% were receiving warfarin and the remaining 91.9% were receiv-

Table 1. Clinical characteristics of the study population according to the type of oral anticoagulant (direct oral anticoagulant vs vitamin K antagonist).

Variable	Total (n = 1337)	DOAC (n = 587; 43.9%†)	VKA (n = 750; 56.1%‡)	p-value§
Age (years)	75.0 ± 8.9¶	76.1 ± 8.5	75.3 ± 9.2	0.170
Sex, male (%)	55.8	54.5	56.8	0.462
Hypertension (%)	85.3	87.5	83.6	0.045
Prior ischemic stroke (%)	60.8	71.2	52.6	0.000
Heart failure (%)	25.7	22.9	27.9	0.041
COPD (%)	16.1	13.3	18.3	0.020
eGFR (ml/min/1.73 m^2):	64.6 ± 19.6¶	66.9 ± 19.5	61.8 ± 20.6	0.000
– <30 ml/min/1.73 m^2 (%)	3.6	1.9	5	0.003
– 31–59 ml/min/1.73 m^2 (%)	29	24.4	32.7	0.001
– ≥60 ml/min/1.73 m^2 (%)	66.8	73	61.8	0.000
Mean $CHADS_2$ score	3.2 ± 1.3¶	3.4 ± 1.2	3 ± 1.3	0.000
Mean CHA_2DS_2-VASC score	4.8 ± 1.5¶	5.03 ± 1.4	4.6 ± 1.5	0.000
Mean HAS-BLED score	2.0 ± 0.9¶	2.5 ± 1.3	2.6 ± 1.5	0.776
Charlson comorbidity index	2.0 ± 1.6¶	2.2 ± 1.7	2 ± 1.6	0.042
Polypathology (%)	38.9	42.5	43.1	0.882
Dementia (%)	3.2	3.4	3.1	0.807
Anemia (%)	14.2	15.2	13.3	0.339
No dependency (%)	71	68.5	73	0.068
Partial dependency (%)	25	27.2	23.3	0.087
Total dependency (%)	4	4.3	3.8	0.652

†27.9% of patients were taking dabigatran, 42.6% rivaroxaban and 29.5% apixaban.
‡91.9% of patients were taking acenocoumarol and 8.1% warfarin.
§p-value of DOAC versus VKA.
¶Mean ± standard deviation.
COPD: Chronic obstructive pulmonary disease; DOAC: Direct oral anticoagulant; eGFR: Estimated glomerular filtration rate; VKA: Vitamin K antagonist.

Table 2. Clinical characteristics according to the type of direct oral anticoagulant.

Variable	Dabigatran (n = 163)	Rivaroxaban (n = 249)	Apixaban (n = 173)	p-value†
Age (years)	75.9 ± 8.3‡	75.6 ± 9.4	76.3 ± 7.6	0.314
Sex, male (%)	55.6	53.7	55.2	0.913
Prior ischemic stroke (%)	78.4	64.4	74	0.006
eGFR (ml/min/1.73 m²):	70 ± 18.4‡	67.7 ± 20.3	64.3 ± 22	0.005
– <30 ml/min/1.73 m² (%)	0.6	1.6	3.5	0.151
– 31–59 ml/min/1.73 m² (%)	17.6	24.1	30.8	0.02
– ≥60 ml/min/1.73 m² (%)	81.8	73.5	64.5	0.002
Mean $CHADS_2$ score	3.4 ± 1.2‡	3.3 ± 1.1	3.5 ± 1.2	0.067
Mean CHA_2DS_2-VASC score	5.1 ± 1.5‡	4.9 ± 1.4	5.1 ± 1.5	0.235
Mean HAS-BLED score	2.6 ± 1.3‡	2.4 ± 1.3	2.4 ± 1.1	0.449
Charlson comorbidity index	2.3 ± 1.8‡	2.1 ± 1.7	2.3 ± 1.7	0.089
Polymedication	81.6	78.3	82.7	0.497
Antiplatelet drugs (%)	14.8	5.2	7.6	0.003
Gastric and duodenal ulcers (%)	2.0	5.8	8.5	0.037
Anemia (%)	11.3	14.3	20.2	0.073

†p-value of dabigatran versus rivaroxaban versus apixaban.
‡Mean ± standard deviation.
DOAC: Direct oral anticoagulant; eGFR: Estimated glomerular filtration rate.

ing acenocoumarol. The mean HAS-BLED score was higher in patients taking acenocoumarol (2.65 ± 1.49 vs 2.29 ± 1.43; $p < 0.05$), although hypertension was more common in patients taking warfarin (93.3% vs 82.9%; $p < 0.05$). No other significant differences were found between the groups.

The mean percent time in the therapeutic range among patients taking VKAs was 56.0 ± 23.8% according to the direct method and 60.3 ± 26.1% according to the Rosendaal method. Patients with a shorter time in the therapeutic range had a higher mean HAS-BLED score ($p < 0.001$).

Analysis of the clinical characteristics of patients according to the type of DOAC (rivaroxaban vs apixaban vs dabigatran) revealed that a history of ischemic stroke, concomitant use of antiplatelet drugs and estimated glomerular filtration rate ≥60 ml/min/1.73 m² were more common in patients taking dabigatran (Table 2). The presence of gastric and duodenal ulcers was more frequent in patients taking apixaban.

The mean SAT-Q score was 63.8 ± 17.8 (54.7 ± 20.1 on the Effectiveness scale and 82.5 ± 17.3 on the Convenience scale). The mean total EQ-5D-3L score was 75.6 ± 20.9 and the visual analog scale score was 63.1 ± 20.6. At the time of the visit, the ACTS Burdens score was 51.8 ± 8.4 and the ACTS Benefits score was 11.9 ± 2.4.

As for satisfaction, the ACTS Burdens score was higher in patients from the neurology department, in patients taking DOACs and in patients with no polypathology, history of stroke, higher estimated glomerular filtration rate and higher $CHADS_2$, CHA_2DS_2-VASC and HAS-BLED scores (Table 3). The ACTS Benefits score was higher in patients taking DOACs than in patients taking VKAs.

The logistic regression analysis performed with data from the SAT-Q showed that the variables associated with greater satisfaction were treatment with DOACs, care in an internal medicine department and higher scores in both the ACTS Burdens and the ACTS Benefits scales (Table 4). Propensity score matching based on the multivariate analysis was performed to minimize potential selection bias (OR: 1.07; 95% CI: 1.003–1.15; $p = 0.042$).

Analysis of satisfaction according to the type of oral anticoagulant based on the SAT-Q questionnaire, the ACTS Burdens scale and the ACTS Benefits scale showed that satisfaction was greater in patients taking DOACs (Table 5). According to the EQ-5D-3L questionnaire, patients taking VKAs with a longer time in the therapeutic range (Rosendaal method) were more satisfied (77.91 ± 19.88 vs 72.79 ± 21.19; $p < 0.05$). Finally, among patients taking DOACs, satisfaction with treatment was independent of the type of DOAC (Table 6). However, 81.3% of physicians considered that compared with the twice-daily dose, taking medication only once daily was important or very important.

Discussion

Clinical trials and observational studies have focused mainly on analyzing the efficacy (reduction of thromboembolic complications) and safety (risk of bleeding) of antithrombotic therapy, but not on satisfaction, quality of life or perception of the burdens and benefits of

Table 3. Variables associated with satisfaction according to the ACTS Burdens scale and ACTS Benefits scale.

Variables	ACTS burdens (Mean ± SD; p- value†)	ACTS benefits Mean ± SD; p-value†)
Department:		
– Neurology department	53.38 ± 7.14	11.92 ± 2.49
– Internal medicine department	49.01 ± 9.67	11.78 ± 2.36
	0.000	0.112
Type of oral anticoagulant:		
– DOAC	54.83 ± 6.11	12.36 ± 2.34
– VKA	49.50 ± 9.15	11.48 ± 2.46
	0.000	0.000
$CHADS_2$:		
– 0–1	50.26 ± 8.71	11.55 ± 2.42
– 2	50.70 ± 8.88	11.88 ± 2.25
– >2	52.17 ± 8.25	11.90 ± 2.44
	0.02	0.363
CHA_2DS_2-VASC:		
– 0–2	49.34 ± 9.37	11.70 ± 2.36
– 3	50.96 ± 8.83	12.04 ± 2.35
– >3	52.14 ± 8.28	11.88 ± 2.44
	0.005	0.516
HAS-BLED:		
– 0–1	50.49 ± 9.03	11.82 ± 2.34
– 2–3	52.53 ± 8.02	11.92 ± 2.48
– >3	49.69 ± 8.71	11.71 ± 2.10
	0.000	0.385
Polypathology:		
– No	52.59 ± 7.98	11.91 ± 2.45
– Yes	51.18 ± 8.41	11.87 ± 2.32
	0.02	0.379
eGFR (ml/min/1.73 m^2):		
– <30	48.42 ± 8.71	11.67 ± 2.11
– 30–59	51.19 ± 8.56	11.73 ± 2.39
– ≥60	52.25 ± 8.29	11.94 ± 2.48
	0.01	0.097
Prior stroke:		
– No	50.20 ± 9.33	11.79 ± 2.37
– Yes	52.92 ± 7.55	11.91 ± 2.5
	0.000	0.224

†p-value between the previous rows.
DOAC: Direct oral anticoagulant; eGFR: Estimated glomerular filtration rate; SD: Standard deviation; VKA: Vitamin K antagonist.

Table 4. Factors associated with satisfaction with treatment according to the SAT-Q (logistic regression analysis).

Variables	Odds ratio	95% CI	Regression coefficient	p-value
DOACs[†]	1.07	1.003–1.15	0.07	0.042
ACTS Benefits scale	1. 64	1.46–1.84	0.49	<0.001
Neurology department	0.64	0.43–0.96	-0.45	0.032
ACTS Burdens scale	1.11	1.07–1.15	0.10	<0.001

[†]Estimation of treatment effect adjusted by Propensity Score Matching.
ACTS: Anti-Clot Treatment Scale; DOAC: Direct oral anticoagulant.

anticoagulants [7]. Importantly, the preferences of patients regarding their antithrombotic therapy should also be considered when selecting the most appropriate treatment. Interestingly, the impact of patients' preferences on the treatment of AF has been analyzed [14,15].

We studied more than 1300 outpatients with NVAF treated with oral anticoagulants in neurology and internal medicine departments in Spain. Compared with other observational studies, the patients in our study had a worse clinical profile, with a higher risk of thromboembolic and bleeding events [16,17]. These differences could be explained by the fact that the patients were recruited only from neurology and internal medicine departments. The interest of our data lies in the fact that these patients have more risk factors and comorbidities. With regard to the type of oral anticoagulant, our data showed that DOACs were prescribed more frequently than VKAs in patients with a history of stroke and in patients with a higher thromboembolic risk. Compared with warfarin, DOACs significantly reduce the risk of stroke and systemic embolic events by 19%, the risk of hemorrhagic stroke by 51% and the risk of intracranial hemorrhage by 52% [8]. Since patients with a history of stroke and patients with higher $CHADS_2$ and CHA_2DS_2-VASC scores are at the highest risk of recurrence [4], it is not surprising that DOACs were more commonly prescribed in this population.

Consistent with prescription patterns in Spain, acenocoumarol was the most commonly prescribed VKA. Mean percent time in the therapeutic range for patients taking VKAs was approximately 56–60%. The various studies that have analyzed control of anticoagulation in patients with NVAF taking VKAs show that anticoagulation control rates are similar to those we detected [16,18–20]. Of note, patients with a longer time in the therapeutic range (Rosendaal method) were more satisfied according to the EQ-5D-3L questionnaire. The association between better control of INR and better quality of life has also been reported by other authors [21,22].

We analyzed clinical characteristics according to the type of DOAC. Recent studies, such as XANTUS or the Dresden DOAC registry, analyzed the use of DOACs in clinical practice [23–27]. Compared with these studies, we found a higher risk of stroke, possibly because patients who attend the neurology and internal medicine departments are at a greater risk and require more complex clinical management.

Our study specifically analyzed satisfaction, quality of life and patients' perception of the burdens and benefits of oral anticoagulants. We found that both satisfaction with oral anticoagulation and quality of life were high. Quality of life associated with anticoagulation therapy diminishes after initiation of therapy, although it improves in the long term [28]. Similarly, short-term anticoagulation therapy (<1 year) has been associated with poorer quality of life [29]. In our study, mean time on anticoagulants was approximately 37 months.

The ACTS Burdens score was higher in individuals with a higher thromboembolic risk. This is not surprising, since these patients may benefit more from anticoagulant therapy [3].

Table 5. Anti-Clot Treatment Scale, SAT-Q and EQ-5D-3L scores according to the type of oral anticoagulant.

Variables	TOTAL (n = 1337)[†]	DOACs (n = 587)[†]	VKAs (n = 750)[†]	p-value[‡]
Mean SAT-Q score	63.79 ± 17.75	70.21 ± 14.87	58.72 ± 18.20	<0.001
Mean EQ-5D-3L score	75.58 ± 20.88	76.26 ± 20.63	75.05 ± 21.07	0.297
Mean ACTS Burdens score	51.84 ± 8.38	54.8 ± 6.1	49.5 ± 9.2	<0.001
Mean ACTS Benefits score	11.87 ± 2.45	12.4 ± 2.3	11.5 ± 2.5	<0.001

[†]Mean ± standard deviation.
[‡]p-value of DOACs versus VKA.
DOAC: Direct oral anticoagulant; VKA: Vitamin K antagonist.

Table 6. ACTS, SAT-Q and EQ-5D-3L scores according to direct oral anticoagulant.

Variables	Dabigatran†	Rivaroxaban†	Apixaban†	p-value
Mean SAT-Q score	69.7 ± 15.63	70.62 ± 13.69	69.62 ± 15.91	0.879
Mean EQ-5D-3L score	74.75 ± 19.86	78.33 ± 20.79	75.06 ± 21.04	0.065
Mean ACTS Burdens score	55.54 ± 5.33	54.58 ± 6.24	54.36 ± 6.82	0.299
Mean ACTS Benefits score	12.26 ± 2.48	12.42 ± 2.13	12.33 ± 2.53	0.918

†Mean ± standard deviation.

Ynsaurriaga *et al.* [7] found that quality of life was impaired by AF, particularly in patients taking anticoagulation therapy [7]. However, the patients studied were taking VKAs. DOACs have relevant advantages over VKAs and this could lead to improved quality of life in patients with AF. In our study, the ACTS Burdens and ACTS Benefits scales and the logistic regression analysis showed that satisfaction was greater with DOACs than with VKAs. In recent years, small-scale studies have suggested that DOACs are associated with a better quality of life than VKAs [30–32]. In a study of 80 patients, mean ACTS Burden scores were more favorable in patients with AF receiving nonwarfarin thromboprophylaxis than in those receiving warfarin-based prophylaxis [33]. In the XANTUS-ACTS substudy, switching from a VKA to rivaroxaban (n = 1291) yielded statistically and clinically significant improvements in the ACTS Burdens and Benefits scores [34]. In a study of 200 patients treated with VKAs, up to 65% of patients stated that they would change to DOACs, particularly those who were less satisfied with their current treatment. No requirement for regular laboratory monitoring and a lower risk of bleeding were the most important arguments for switching to a DOAC [35]. In contrast, in another study, patients considered efficacy to be more important than safety and both considerably more important than convenience-related factors (blood tests, dose frequency and interactions with drugs and food). Cost of treatment was also taken into account [36]. Therefore, many factors could impact satisfaction and should be considered when prescribing an oral anticoagulant. This is particularly relevant in polymedicated elderly patients [13]. In a large sample of patients, we found that satisfaction and quality of life were higher with DOACs than with VKAs. The use of VKAs, but not DOACs, implies relevant behavior and lifestyle modifications that may have a negative impact on quality of life [7]. In addition, not maintaining INR levels close to recommended targets has been associated with increased anxiety and poorer quality of life, particularly when variations are high [37]. No significant differences were observed for quality of life with DOACs. However, our study was not specifically designed for this purpose. In summary, the quality of life of patients with AF receiving anticoagulation therapy, including frail patients with polypathology, is improved by DOACs.

Finally, although satisfaction with treatment was independent of the type of DOAC, more than 80% of physicians considered that compared with twice daily dosing, taking medication once daily was important or very important. In patients with chronic conditions, treatment must be simplified to improve adherence. It has been reported that patients with AF seem to prefer treatment options which are easier to administer [38]. Thus, in patients with NVAF, once daily dosing regimens for chronic medications are associated with an approximately 26% higher likelihood of adherence than twice-daily regimens [39].

Since this study was performed in NVAF patients attended in neurology or internal medicine departments in Spain, the conclusions can only be extended to patients with a similar clinical profile and healthcare system. Thus, our data can be extended to patients with polypathology, comorbidities associated with advanced age or a history of stroke. Nevertheless, we performed propensity score matching to reduce potential selection bias. The other limitations of the present study were addressed in a study of the validation of the ACTS SAT-Q [9].

Conclusion

Satisfaction and quality of life were better in patients taking DOACs. Being attended in the internal medicine department and achieving higher scores in both the ACTS Burdens and ACTS Benefits scales were associated with greater satisfaction. Most physicians considered that compared with twice-daily dosing, taking medication only once daily was important or very important.

Investigators

Antonio Pose, José Antonio Díaz, Manuel Rodríguez, Marta Pena, Susana Arias, Davinia Larrosa, Álvaro González, Elisa Rodríguez, Montserrat González, Dolores Fernández, Cristina Barbagelata, Natividad Raña, Santiago Freire, J Manuel Cerqueiro, Héctor Guerrero, Laura Ramos, Leticia Álvarez, José Mª de Lis, Carmen Caro, Manuel Seijo, Susana Mederer, Miguel Alberto

de Zarraga, José Ferreiro, José Mª Terrero, Mónica Arias, Roberto Pérez, Joaquín Sánchez, José Maciñeiras, Julián Fernández, Fernando Jaén, David Esteva, Mónica Zamora, Nuria Navarrete, Javier García, Luis Mérida, Miguel Ángel Corrales, Raúl Quirós, Jesús Cantero, Fco Javier Barrero, Inmaculada Villegas, José Castro, Jesús Foronda, Dionisio Carrillo, Jesús Vega, José Antonio Trujillo, Manuel Montero, Ana Jurado, Carlos Sánchez, Eduardo Agüera-Morales, María Sánchez, Purificación Durán, Rafael Fernández de la Puerta, María Pérez de la Blanca, María Paz Martínez, Óscar Fernández, José Antonio Tamayo, Rafael Bustamante, Pedro Jesús Serrano, Antonio Arjona, Javier Fernández, Manuel Payan, Ricardo Gómez, Daniel Peña, Enrique Cabrerizo, Fernando Salgado, Radka Ivanova Georgieva, Antonio Gil-Núñez, Elena Bello, Fernando Díaz, Antonio Medina, Ana Castellano, Yesica Miranda, Óscar Fabre, Iluminada García Polo, Patricia Ibáñez, Clara Sainz, Fernando Sierra, Esther Aragón, Jaime Díaz, Fernando Aguilar, María Ángeles Ortega, José Antonio Egido, José Carlos Pontes, Miguel Ángel García, Francisco Cabrera, Blanca Batalla, Alex Culla, Carlos Molina, Alan Flores, Laia Seró, Marian Muchada, Pilar Meler, Sandra Boned-Riera, David Cánovas, Jordi Estela, Juli Font, Francisco Purroy, Ikram Benabdelhak, Jordi Sanahuja, Jaume Roquer, Ana Rodríguez, Ángel Ois, Elisa Cuadrado, Jordi Jiménez, Xavier Nogués, Jerzy Kuprinski, Antoni German, Daniel Irigoyen, Juan José Cara, María Angels Font, Sonia Huertas, Alejandro Martínez-Domeño, Juan Antonio Arroyo, Raquel Delgado-Mederos, Manuel Jesús Gómez-Choco, Juan José Mengual, Sonia Mª García, Mª del Mar Castellanos, Cecile Van Eedenburg, Imma Cañas, Jordi Espinosa, Santiago Montull, Helena Quesada, Xavier Ustrell, Christian Homedes, Irene Navalpotro, Jordi Casanova, Aida Pilar Lago, Carmen Morata, David Gorriz, Iván Moreno, José Tembl, Alejandro Ponz, Mª José Fonseca, Raquel Chamarro, Rosario Gil, Vicente Oliver, Ana Pampliega, Arturo Artero, Francesc Puchades, Lamberto Landete, Carlos Vilar, Carmen Jiménez, Bárbara Vives, Mª Dolores Moragues, Rosa Díaz, Silvia Tur, José Bernardo Escribano, César Lucas, Francisco Martínez, José Miguel Pons, Amparo Romero, David García, José Pérez, Ramón Villaverde, Salvadora Martínez, Aida Rodríguez, Carlos Tejero, Cristina Pérez, Enrique Mostacero, Covadonga Fernández, Alain Luna, Tomás Pérez, Félix González, Ana de Arce, Maite Martínez, Noemí Díez, Jaime Gállego, Beatriz Zandio, María Herrera, Nuria Aymerich, Roberto Muñoz, Javier Marta, Jorge Artal, José Mª Errea, Juan José Timiraos, Mª Pilar Moreno, Mar Freijo, Juan Manuel García, Mª Carmen Gil, Mª Ángeles Revilla, Enrique Palacio, José Luis Vázquez, María Bestué, Ana Latorre, Eva Calvo, Laura Ballester, Marta Serrano, Jesús Mª Juega, Mª Ángeles López, Pablo Irimia, Laura Imaz, Blanca Fuentes, Borja Enrique Sanz, Luis Beltrán, Gerardo Ruiz, Patricia Martínez, Demetrio Sánchez, Emilio Barroso, Igor Molina, Marco Antonio Budiño, Jaime Masjuan, Alicia de Felipe, Consuelo Matute, Javier Tejada, Alberto Morán, Esther Fernández, Mª del Carmen Riveira, Joaquín Carnedo, Antonio Manquillo, Raquel González, José Carlos Fernández, Marta Guillan, Miguel Yebra, José Mª Trejo, Jesús Saiz, Juan Carlos Martínez-Acitores, Yolanda Bravo, Juan Francisco Arenillas, Ana Calleja, Elisa Cortijo, Javier Reyes, Luis López, Pedro Luis Muñoz, Mª Ángeles Fidalgo, Jacinto Hernández, José Carlos Gómez, José Carlos Morán, Sonia Gonzalo, Jorge Marrero, José Ángel Satué, Juan Carlos Belinchón, Francisco Moniche, Enrique Calderón, Irene Escudero, Javier de la Torre, Ignacio Casado, Joaquín Antón, Juan Carlos Portilla, Juan Luengo, Joan Rosal, Elena Calzado, Juan Carlos Anglada, Juan Girón, José Mª Ramírez, Agustín Pijierro, Ana Roa, Jorge Romero, Mariano Aguayo, Cristina Borrachero, Gema Sanz, Mª José Gómez, Miguel Ángel Rico, Antonio Cayon, Eduardo Carmona, Román Cerro, Rafael López, Alfonso Aguirre, Francisco Lozano, José Mª Rivera.

Acknowledgements

The authors thank LV Piris (Methodology Unit of IIS-La Princesa) for help with the statistical analysis.

Financial & competing interests disclosure

J Vivancos and CS Fernández are the co-ordinators of the ALADIN study. This study was supported by a grant from Bayer. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Editorial assistance was provided by Content Ed Net, Madrid, Spain with funding from Bayer Hispania.

Ethical conduct of research

All data used to perform this analysis were de-identified and accessed in compliance with the Health Insurance Portability and Accountability Act. As a retrospective analysis of a de-identified database, the research was exempted from IRB review under 45 CFR 46.101(b)(4). The research was conducted according to the principles of the Declaration of Helsinki.

Summary points

- Patients with nonvalvular atrial fibrillation treated with oral anticoagulants attended in neurology and internal medicine departments in Spain had many comorbidities and a high thromboembolic risk.
- Satisfaction and quality of life with oral anticoagulants were high and were better with direct oral anticoagulants than with vitamin K antagonist.
- Being attended in the internal medicine department and achieving higher scores in both the Anti-Clot Treatment Burdens and the Anti-Clot Treatment Benefits scales were associated with greater satisfaction.
- Most physicians considered that compared with twice daily dosing, taking medication only once daily was important or very important.

References

1 Rahman F, Kwan GF, Benjamin EJ. Global epidemiology of atrial fibrillation. *Nat. Rev. Cardiol.* 11, 639–654 (2014).

2 Barrios V, Calderon A, Escobar C, De la Figuera M. Patients with atrial fibrillation in a primary care setting: Val-FAAP study. *Rev. Esp. Cardiol. (Engl. Ed.)* 65, 47–53 (2012).

3 Camm AJ, Lip GYH, De Caterina R *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. *Eur. Heart J.* 33, 2719–2747 (2012).

4 Masjuán J, Álvarez-Sabín J, Blanco M *et al.* [Current management of antithrombotic treatment in patients with non valvular atrial fibrillation and prior history of stroke or transient ischemic attack]. *Rev. Neurol.* 59, 25–36 (2014).

5 Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann. Intern. Med.* 146, 857–867 (2007).

6 Barrios V, Escobar C. Rivaroxaban: a once-daily anticoagulant for the prevention of thromboembolic complications. *Expert Rev. Cardiovasc. Ther.* 11, 129–141 (2013).

7 Ynsaurriaga FA, Peinado RP, Ormaetxe Merodio JM. Atrial fibrillation and quality of life related to disease and treatment: focus on anticoagulation. *Future Cardiol.* 10, 381–393 (2014).

8 Ruff CT, Giugliano RP, Braunwald E *et al.* Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 383, 955–962 (2014).

9 Suárez C, Pose A, Montero-Pérez-Barquero M *et al.* [Validation of satisfaction questionnaire ACTS in outpatients with atrial fibrillation treated with oral anticoagulants attended in Spain. ALADIN study]. *Med. Clin. (Barc).* 147, 192–198 (2016).

10 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J. Chronic Dis.* 40, 373–383 (1987).

11 SEMI, semFYC, FAECAP. Care process of patients with complex chronic diseases and pluripathology. www.fesemi.org/documentos/1385470163/publicaciones

12 Rosendaal FR, Cannegieter SC, van der Meer FJ, Briët E. A method to determine the optimal intensity of oral anticoagulant therapy. *Thromb. Haemost.* 69, 236–239 (1993).

13 Cano SJ, Lamping DL, Bamber L, Smith S. The anti-clot treatment scale (ACTS) in clinical trials: cross-cultural validation in venous thromboembolism patients. *Health Qual. Life Outcomes* 10, 120 (2012).

14 Protheroe J, Fahey T, Montgomery AA, Peters TJ. Effects of patients' preferences on the treatment of atrial fibrillation: observational study of patient-based decision analysis. *West. J. Med.* 174, 311–315 (2001).

15 Man-Son-Hing M, Gage BF, Montgomery AA *et al.* Preference-based antithrombotic therapy in atrial fibrillation: implications for clinical decision making. *Med. Decis. Making* 25, 548–559 (2005).

16 Barrios V, Escobar C, Prieto L *et al.* Anticoagulation control in patients with nonvalvular atrial fibrillation attended at primary care centers in spain: the PAULA study. *Rev. Esp. Cardiol. (Engl. Ed.)* 68, 769–776 (2015).

17 Lip GY, Rushton-Smith SK, Goldhaber SZ *et al.* GARFIELD-AF Investigators. Does sex affect anticoagulant use for stroke prevention in nonvalvular atrial fibrillation? The prospective global anticoagulant registry in the FIELD-atrial fibrillation. *Circ. Cardiovasc. Qual. Outcomes* 8(2 Suppl. 1), S12–S20 (2015).

18 Bertomeu-González V, Anguita M, Moreno-Arribas J *et al.* Quality of anticoagulation with vitamin K antagonists. *Clin. Cardiol.* 38, 357–364 (2015).

19 Razouki Z, Ozonoff A, Zhao S, Rose AJ. Pathways to poor anticoagulation control. *J. Thromb. Haemost.* 12, 628–634 (2014).

20 Costa GL, Lamego RM, Colosimo EA, Valacio RA, Moreira Mda C. Identifying potential predictors of high-quality oral anticoagulation assessed by time in therapeutic international normalized ratio range: a prospective, long-term, single-center, observational study. *Clin. Ther.* 34, 1511–1520 (2012).

21 Hasan SS, Teh KM, Ahmed SI, Chong DW, Ong HC, Naina B. Quality of life (QoL) and International Normalized Ratio (INR) control of patients attending anticoagulation clinics. *Public Health* 129, 954–962 (2015).

22 Wang Y, Kong MC, Lee LH, Ng HJ, Ko Y. Knowledge, satisfaction, and concerns regarding warfarin therapy and their association with warfarin adherence and anticoagulation control. *Thromb. Res.* 133, 550–554 (2014).

23 Camm AJ, Amarenco P, Haas S *et al.*; XANTUS Investigators. XANTUS: a real-world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation. *Eur. Heart J.* 37, 1145–1153 (2016).

24 Beyer-Westendorf J, Förster K, Pannach S *et al.* Rates, management, and outcome of rivaroxaban bleeding in daily care: results from the Dresden DOAC registry. *Blood* 124, 955–962 (2014).

25 Beyer-Westendorf J, Ebertz F, Förster K *et al.* Effectiveness and safety of dabigatran therapy in daily-care patients with atrial fibrillation. Results from the Dresden DOAC Registry. *Thromb. Haemost.* 113, 1247–1257 (2015).

26 Álvarez-Otero J, de la Fuente-Aguado J, Arias-Castaño JC, González-González L, Puerta-Louro R, Araújo-Fernández S. [Dabigatran: experience in standard clinical practice]. *Rev. Clin. Esp.* 215, 385–390 (2015).

27 Beyer-Westendorf J, Werth S, Tittl L, Michalski F, Marten S, Weiss N. Real life efficacy and safety of apixaban for stroke prevention in atrial fibrillation – results of the prospective DOAC registry (NCT01588119). Presented at: *The XXV Congress of the International Society on Thrombosis and Haemostasis*. Toronto, Canada, 20–25 June 2015 (Abstract: AS098).

28 Marvig CL, Verhoef TI, de Boer A *et al.* Quality of life in patients with venous thromboembolism and atrial fibrillation

treated with coumarin anticoagulants. *Thromb. Res.* 136, 69–75 (2015).

29 Corbi IS, Dantas RA, Pelegrino FM, Carvalho AR. Health related quality of life of patients undergoing oral anticoagulation therapy. *Rev. Lat. Am. Enfermagem.* 19, 865–873 (2011).

30 Turker Y, Ekinozu I, Aytekin S *et al.* Comparison of changes in anxiety and depression level between dabigatran and warfarin use in patients with atrial fibrillation. *Clin. Appl. Thromb. Hemost.* 23(2), 164–167 (2017).

31 Fareau S, Baumstarck K, Farcet A, Molines C, Auquier P, Retornaz F. [Quality of life of elderly people on oral anticoagulant for atrial fibrillation: VKA versus direct oral anticoagulants]. *Geriatr. Psychol. Neuropsychiatr. Vieil.* 13, 45–54 (2015).

32 Alegret JM, Viñolas X, Arias MA *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.* 11, 680–684 (2014).

33 Coleman CI, Coleman SM, Vanderpoel J *et al.* Patient satisfaction with warfarin- and non-warfarin-containing thromboprophylaxis regimens for atrial fibrillation. *J. Investig. Med.* 61, 878–881 (2013).

34 Coleman CI, Haas S, Turpie AG *et al.* Impact of switching from vitamin K antagonist to rivaroxaban on satisfaction with anticoagulation therapy: the XANTUS-ACTS substudy. *Clin. Cardiol.* 39(10), 565–569 (2016).

35 Boom MS, Berghuis EM, Nieuwkerk PT, Pinedo S, Büller HR. When do patients prefer a direct oral anticoagulant over a vitamin K antagonist? *Neth. J. Med.* 73, 368–372 (2015).

36 Ghijben P, Lancsar E, Zavarsek S. Preferences for oral anticoagulants in atrial fibrillation: a best-best discrete choice experiment. *Pharmacoeconomics* 32, 1115–1127 (2014).

37 Soliman Hamad MA, van Eekelen E, van Agt T, van Straten AH. Self-management program improves anticoagulation control and quality of life: a prospective randomized study. *Eur. J. Cardiothorac. Surg.* 35, 265–269 (2009).

38 Böttger B, Thate-Waschke IM, Bauersachs R, Kohlmann T, Wilke T. Preferences for anticoagulation therapy in atrial fibrillation: the patients' view. *J. Thromb. Thrombolysis* 40, 406–415 (2015).

39 Laliberté F, Nelson WW, Lefebvre P, Schein JR, Rondeau-Leclaire J, Duh MS. Impact of daily dosing frequency on adherence to chronic medications among nonvalvular atrial fibrillation patients. *Adv. Ther.* 29, 675–690 (2012).