European Journal of Clinical Investigation. 2018; 48(5): e12910

Relation of quality of anticoagulation control with different management systems among patients with atrial fibrillation: Data from FANTASIIA Registry

Inmaculada Roldán Rabadán[1], María Asunción Esteve-Pastor[2], Manuel Anguita-Sánchez[3], Javier Muñiz[4], José Camacho Siles[5] María Angustias Quesada[5], Martín Ruiz Ortiz[3], Francisco Marín[2], Manuel Martínez Sellés[6], Vicente Bertomeu[7], Gregory Y.H. Lip[8,9], Angel Cequier Fillat[10], Lina Badimón[11], on behalf of the FANTASIIA Study Investigators

1 Department of Cardiology, Hospital Universitario La Paz, Instituto de Investigación de La Paz (IDIPAZ), CIBER-CV, Madrid, Spain
2 Department of Cardiology, Hospital Clínico Universitario Virgen de la Arrixaca, Instituto Murciano de Investigación Biosanitaria (IMIB-Arrixaca), CIBER-CV, Murcia, Spain
3 Department of Cardiology, Hospital Universitario Reina Sofía, Córdoba, Spain
4 Instituto Universitario de Ciencias de la Salud, Instituto de Investigación Biomédica de A Coruña (INIBIC), Universidade da Coruña, CIBER-CV, A Coruña, Spain
5 Department of Internal Medicine, Hospital Universitario La Paz, Madrid, Spain
6 Department of Cardiology, Hospital Universitario Gregorio Marañón , Complutense University, European University of Madrid, CIBER-CV, Madrid, Spain
7 Department of Cardiology, Hospital Universitario de San Juan, CIBER-CV, Alicante, Spain
8 Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, United Kingdom
9 Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark
10 Department of Cardiology, Hospital de Bellvitge, CIBER-CV, Barcelona, Spain
11 Cardiovascular Research Center, CSIC-ICCC, Hospital de la Santa Creu i Sant Pau, IIB-Sant Pau, CIBER-CV, Barcelona, Spain

Abstract
Background. Anticoagulation control in patients with atrial fibrillation (AF) has a multidisciplinary approach although is usually managed by general practitioners (GP) or haematologists. The aim of our study was to assess the quality of anticoagulation control with vitamin K antagonists (VKAs) in relation to the responsible specialist in a "real-world" AF population.
Methods. We consecutively enrolled VKA anticoagulated patients included in the FANTASIIA Registry from 2013 to 2015. We analysed demographical, clinical characteristics and the quality of anticoagulation control according to the specialist responsible (ie GPs or haematologists).
Results. Data on 1584 patients were included (42.5% females, mean age 74.0 ± 9.4 years): 977 (61.7%) patients were controlled by GPs and 607 (38.3%) by haematologists. Patients managed by GPs had higher previous heart disease (53.2% vs 43.3%, $P < .001$), heart failure (32.9% vs 26.5%, $P < .008$) and dilated cardiomyopathy (15.2% vs 8.7%, $P < .001$) with better renal function (69.3 ± 24.7 vs 63.1 ± 21.4 mL/min, $P < .001$) compared to patients managed by haematologists. There was no difference between groups in the type of AF, CHA_2DS_2-VASc or HAS-BLED scores, but patients with electrical cardioversion were more prevalent in GP group. The overall mean time in therapeutic range (TTR) assessed by Rosendaal method was 61.5 ± 24.9%; 52.6% of patients had TTR<65% and 60% of patients had TTR<70%. TTR was significantly lower in patients controlled by haematologists than by GPs (63 ± 24.4 vs 59.2 ± 25.6, $P < .005$).
Conclusions. About 60% of AF patients anticoagulated with VKAs had poor anticoagulation control (ie TTR<70%), and their management was only slightly better than when it is managed by general practitioners.

Keywords
Anticoagulation quality, atrial fibrillation, general practitioners, haematologists

Funding Information. The FANTASIIA registry was funded by an unconditional grant from Pfizer/Bristol-Myers-Squibb and by grants from the Instituto de Salud Carlos III (Madrid)-FEDER (RD12/0042/0068, RD12/0042/0010, RD12/0042/0069, PI13/00513 and RD12/0042/0063).

1. INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia in developed countries[1-3] and is associated with an increased mortality and morbidity rate, with an associated hospitalisation and healthcare costs.[2, 4-10] Therefore, it is essential to ensure optimal and homogeneous management, with emphasis on quality of anticoagulation. Whilst well-managed anticoagulation reduced stroke and mortality, poor anticoagulation control leads an increase in thrombotic and bleeding events, as well as mortality.[11]

Atrial fibrillation management is performed by various medical specialists, but anticoagulation control is usually managed by the general practitioner (GP) or haematologist and, in a smaller number of cases, by cardiologists or internists. To achieve a good control of the quality of anticoagulation requires experience and knowledge both by the doctor and the patient. Since 2010, we have seen annual updates of clinical practice guidelines (both European and American) containing new algorithms, use of thrombotic and bleeding risk scores, as well as the introduction of four nonvitamin K oral anticoagulants (NOACs), with a better safety profile. All these updates are useful, but their application in everyday clinical practice is not immediate. For that reason, the management of anticoagulation is not homogeneous among different professionals.

On the other hand, the quality of anticoagulation control is not assessed in a homogeneous way by all groups. This assessment is sometimes the result of using a simple percentage of *international normalised range* (INR) in therapeutic range (PINRR)[12] and, in other cases, by the time in the therapeutic range (TTR) as measured by the Rosendaal method.[13] Although NOACs have emerged as an effective and safe alternative to VKA therapy, treatment with VKA is still a valid option in AF patients.[14] The AuriculA registry from Swedish population showed that in patients who spend high proportion of time in the therapeutic range, the treatment with warfarin is safe and effective and will continue to be a valid option.[15]

The aim of our study was to assess the quality of anticoagulation control with vitamin K antagonists (VKAs) in relation to the responsible specialist in a "real-world" AF population.

2. METHODS

2.1 Study design

The data from this study come from the FANTASIIA Registry ("Fibrilación Auricular: influencia del Nivel y Tipo de Anticoagulación Sobre la incidencia de Ictus y Accidentes hemorrágicos"), a national, multicentric, observational and prospective study which main objective is to evaluate the incidence of thromboembolic and haemorrhagic events in a prospective sample of AF patients over 3 years of follow-up, in relation to the type of antithrombotic agents, VKA or NOACs, and the quality of anticoagulation (in those who receive VKA). The design has been previously published[16] and includes an initial visit and three follow-up visits, after 1, 2 and 3 years, where clinical and laboratory data of patients would be collected in an electronic data notebook. In this study, we assess the quality of anticoagulation control with VKAs in relation to the responsible specialist in a "real-world" AF population: the GP or the haematologist.

2.2 Study population

A total of 1640 consecutive outpatients treated with VKAs were included in the analysis of this study. During the selection process, 56 patients were excluded because the data about the specialist in charge of their anticoagulation control were not available. Therefore, the final analysed sample size was 1584 patients.

Demographic, clinical and analytical variables were collected from all patients in medical records. Previous major bleeding events were defined according to the 2005 International Society of Thrombosis and Haemostasis criteria: fatal bleeding or symptomatic bleeding in a critical anatomical site (intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial or intramuscular with compartment syndrome) and/or bleeding causing a fall in haemoglobin ≥20 g/L or transfusion of ≥2 units of packed red blood cells. Patients with rheumatic mitral valvular disease or prosthetic valve patients were excluded.

For the present analysis, two groups were established according to the specialist responsible of anticoagulation control: GPs or haematologists. In the first case, the control of anticoagulation was performed completely in the primary care centre, by GPs. The blood test was performed with a portable system, and the interpretation and adjustment of the pattern were established by the GPs. The way for the anticoagulation management option with GPs or haematologists depended of the geographical region of the patient (FANTASIIA registry is a multicenter registry that involves 50 centres).

In the case of haematology control, two modalities were observed according to the local care organisation: in the first, only the haematologist was responsible for the complete process of anticoagulation control; and in the second, a blood sample was extracted in the primary care centre, sent to the Hematology laboratory and the haematologist sent the recommendation of the anticoagulation treatment to the GPs who transmitted it to the patient.

The FANTASIIA Registry complies with all the requirements of the Helsinki Declaration, and the study protocol was approved by the Clinical and Ethical Testing Committee of the Hospital Universitario San Juan de Alicante (approval number 12/220) by all Ethics Committees of the participating centres, as well as the Spanish Agency for Medicine and Health Products (SEC-ACO-2012-01 postauthorisation approval code). All the participating patients signed the informed consent. Reporting of the study conforms to STROBE statement along with references to STROBE statement and the broader EQUATOR guidelines.[17]

2.3 Quality of anticoagulation control

All available INR of each patient in the 6 months previous was collected at baseline with at least 1 INR per month to calculate the time in the therapeutic range. The FANTASIIA registry is an observational multicenter registry. For that reason, all the frequency of the INR determinations to maintain the INR between 2.0 and 3.0 and the frequency of visits to the physicians were performed following the usual clinical practice without any additional intervention. Poor quality of anticoagulation or "INR lability" was defined when patients experienced a TTR <65%. The TTR was estimated according to different methods. The main methodology employed was the classical linear method of Rosendaal.[13] However, the quality of anticoagulation also was studied according to the direct method or percentage of INR in therapeutic range (PINRR). This method calculates the TTR according to the number of visits where the INR is in therapeutic range (between 2.0 and 3.0) and divides it by the total number of visits. Similarly, the INR variability was estimated using the Fihn method,[18] evaluating the INR variability using the growth rate of the variance according to the Fihn method. We assessed the quality of anticoagulation therapy following the ESC criteria of the percentage of patients with TTR <70% measured by Rosendaal.

2.4 Statistical analysis

Quantitative variables are described by mean and standard deviation or median and interquartile range based on whether they followed a normal distribution. To test the normal distribution, the Kolmogorov-Smirnov test was used. For comparisons among groups, Student's t test was used in the case of continuous variables and Chi-square in the case of qualitative variables, considering the value of $P < .05$ as statistically significant. We performed a logistic regression analysis to perform the univariate adjustment considering the clinical variables that have been demonstrated a relevant association with poor quality of anticoagulation (age, sex,

hypertension, diabetes mellitus, previous bleeding, heart disease, Charlson index, $CHADS_2$, CHA_2DS_2-VASc, HAS-BLED and specialist responsible of anticoagulation control). A multivariate logistic regression analysis was carried out with those of the relevant variables included in the univariate with a value of $P < .150$. The results are presented as odds ratio (OR) with a 95% confidence interval. STATA statistical version 12.0 was employed for the statistical analysis.

3. RESULTS

3.1 Comparison of baseline characteristics of both groups

Of the 1,584 patients analysed, in 977 (61.7%) had anticoagulation management by GPs and in 607 (38.3%) by haematologists. The mean age was 74.0 ± 9.4 years and 57.3% were male, with no significant differences between groups (Table 1). Comorbidities, risk factors, history of stroke and major haemorrhage appeared similar in both groups, although history of gastrointestinal haemorrhage was higher (3.7% vs 22.7%, $P = .043$) in the group managed by haematologists. All investigations, diagnoses and initial treatments data were similar in both groups. Mean glomerular filtration rate (63.1 ± 21.4 vs 69.4 ± 24.7 mL/min, $P < .001$) and the left ventricular ejection fraction (57.7 ± 11.8% vs 59.3 ± 10.6%, $P = .040$) were marginally better in the group managed by haematologists. More concomitant use of antiplatelet agents (12.5% vs 9.0%, $P = .026$) was observed in the group managed by haematologists.

Table 1. Distribution of baseline clinical characteristics according to the specialist responsible of the anticoagulation control

	Total n = 1584	General practitioner n = 977	Haematologist n = 607	*P*-value
Demographic				
Male sex	909 (57.3)	558 (57.1)	352 (58.0)	.945
Age (y)	74.0 ± 9.4	73.9 ± 9.6	74.2 ± 9.1	.945
Comorbidities				
Hypertension	1,281 (80.9)	782 (80.0)	499 (82.2)	.286
Diabetes mellitus	478 (30.2)	292 (29.9)	187 (30.8)	.698
Dyslipidaemia	851 (53.7)	526 (53.8)	325 (53.5)	.908
Current smoker	81 (5.1)	54 (5.5)	26 (4.3)	.272
Current alcohol	57 (3.6)	35 (3.6)	22 (3.6)	.965
Any heart disease	782 (49.4)	520 (53.2)	263 (43.3)	<.001
COPD	284 (17.9)	189 (19.3)	94 (15.5)	.051
Previous stroke	250 (15.8)	152 (15.6)	98 (16.1)	.755
Extracranial embolism	32 (2.0)	21 (2.1)	12 (2.0)	.923
Malignant disease	150 (9.2)	93 (9.5)	52 (8.6)	.523
PAD	97 (6.1)	64 (6.6)	31 (5.1)	.210
Charlson Index	1.2 ± 1.2	1.2 ± 1.2	1.2 ± 1.1	.087
Chronic kidney disease (eGFR ≤ 60 mL/min)	335 (21.2)	221 (22.6)	114 (18.8)	.069
Hepatic disease	22 (1.4)	17 (1.7)	5 (0.8)	.130
Previous bleeding events				
Major bleeding	55 (3.1)	27 (2.8)	22 (3.6)	.336
ICH	65 (4.1)	36 (3.7)	28 (4.6)	.882
GIB	193 (12.2)	36 (3.7)	138 (22.7)	.043
Haematuria	291 (18.4)	181 (18.5)	110 (18.2)	.976
Any blood transfusion	646 (40.8)	471 (48.2)	193 (31.8)	.247
CHA_2DS_2-VASc score	3.7 ± 1.6	3.7 ± 1.6	3.7 ± 1.5	.408
HAS-BLED score	2.0 ± 1.0	1.9 ± 1.0	2.1 ± 1.1	.070
Concomitant treatment				
Diuretics	942 (59.5)	586 (60.0)	356 (58,79)	.600
ACE inhibitors	518 (32.7)	347 (35.5)	171 (28.2)	.002
ARB	624 (39.4)	349 (35.7)	275 (45.3)	<.001
Statins	869 (54.9)	531 (54.4)	338 (55.7)	.604
Antiplatelet agents	165 (10.4)	88 (9.0)	76 (12.5)	.026
Beta-blockers	961 (60.7)	595 (60.9)	366 (60.3)	.811
Digoxin	303 (19.1)	192 (19.7)	111 (18.3)	.502
Baseline physical examination				
SBP (mm Hg)	132.7 ± 18.8	132.4 ± 19.4	133.1 ± 17.8	.572
DBP (mm Hg)	75.6 ± 11.5	75.4 ± 11.8	75.9 ± 11.0	.311
HR (beats per min)	72,4 ± 14,9	72,5 ± 15,0	72,3 ± 14,8	.795
BMI (Kg/m^2)	29.0 ± 4.9	29.0 ± 5.0	29.1 ± 4.8	.821
LVEF (%)	58.3 ± 11.4	57.7 ± 11.8	59.3 ± 10.6	.045
Haemoglobin (g/dL)	13.7 ± 1.7	13.7 ± 1.7	13.6 ± 1.8	.815
eGFR (mL/min)	65.5 ± 22.9	63.1 ± 21.4	69.4 ± 24.7	<.001
Cholesterol (mg/dL)	177.3 ± 38.9	177.5 ± 39.3	176.9 ± 38.2	.925
Glycaemia (mg/dL)	108.8 ± 32.0	109.3 ± 33.2	107.8 ± 30.1	.386

COPD, chronic obstructive pulmonary disease; PAD, peripheral artery disease; CAD, coronary artery disease; eGFR, estimated glomerular filtrated rate; ICH, intracranial haemorrhage; GIB, gastrointestinal bleeding; ICH, intracranial haemorrhage; ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blockers; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; BMI, body mass index; LVEF, left ventricular ejection fraction.
CHA_2DS_2-VASc = congestive heart failure or left ventricular dysfunction (1); hypertension (1), age ≥ 75 (2) or 65-74 (1), diabetes mellitus (1), prior stroke/TIA or systemic embolism (2), vascular disease (peripheral artery disease, myocardial infarction and aortic plaque) (1), sex category (ie female sex) (1); HAS-BLED = hypertension (1), abnormal renal and/or liver function (1), prior stroke (1), bleeding history or predisposition (1), labile INR (1), elderly (1), drugs or excess alcohol (1).
Numeric values are expressed as median (±standard deviation) or number (percentage).

3.2 Previous heart disease history

Patients in the group controlled by GPs had more previous heart disease (53.2% vs 43.3%, $P < .001$), heart failure (32.9% vs 26.5%, $P = .008$), cardiomyopathy (15.2% vs 8.7%, $P < .001$) and left ventricular hypertrophy due to arterial hypertension (18.1% vs 13.7%, $P = .020$) as well as a higher percentage of cardiac resynchronisation therapy (5.0% vs 1.5%, $P < .001$) (Table S1). Types of AF were similar in both groups, but more electrical cardioversion (19.8% vs 14.7%, $P = .010$) and previous AF ablation procedure (5.2% vs 2.1%, $P = .002$), rhythm control (41.9% vs 34.3%, $P = .003$) and follow-up by cardiology (88.7% vs 86.3%, $P = .002$) were observed in the GP group.

The general population had high thrombotic and haemorrhagic risk, with CHA_2DS_2-VASc mean score of 3.72 ± 1.58 and mean HAS-BLED of 2.01 ± 1.03, with no differences between groups.

3.3 Quality of anticoagulation control in both groups

In the overall population studied, the quality of anticoagulation estimated by TTR by the Rosendaal method was 61.5 ± 24.1%; 52.6% of the patients had a TTR <65% and 60% of the patients had a TTR <70% **(Table 2).** The TTR was significantly higher in the GPs group (63.0 ± 24.4% vs 59.2 ± 25.6%, $P = .005$) with a lower proportion of patients with a TTR <65% (49.7% vs 57.1%, $P = .004$) and TTR <70% (56.8% vs 62.7%, $P = .021$) in the group managed by GPs.

Table 2. Anticoagulation control according to the specialist responsible of the anticoagulation control

	Total n = 1,584	General practitioner n = 977	Haematologist n = 607	*P*-value
TTR (direct method-PINRR)	65.1 ± 24.1	65.9 ± 24.0	63.8 ± 24.3	.068
TTR (Rosendaal)	61.5 ± 24.9	63.0 ± 24.4	59.2 ± 25.6	.005
INR Variability	0.1 ± 0.1	0.1 ± 0.1	0.2 ± 1.0	.279
TTR < 65%	52.6	49.7	57.1	.004
TTR < 70%	60.0	56.8	62.7	.021

TTR, time in therapeutic range assessed by Rosendaal Method; INR, international normalised ratio; PINRR, percentage of international normalised range (INR) in therapeutic range.
Numeric values are expressed as media (± standard deviation) or number (percentage).

After the univariate and multivariate analysis, only the management of anticoagulation according to the type of specialist was independently associated with poor anticoagulation control (TTR <65%) with an OR 1.35 ([95% CI, 1-1.7], *P* = .005). (**Table** 3).

Table 3. Clinical factors related with poor anticoagulation control (TTR 65%) by univariate and multivariate regression analysis

	Univariate analysis OR (95% CI); *P* -value	Multivariate analysis OR (95% CI); *P*-value
Age	1.0 (0.99-1.01); .894	-
Male sex	1.11 (0.91-1.36); .297	-
Hypertension	1.11 (0.86-1.42); .422	-
Chronic kidney disease	1.29 (1.01-1.64); .043	1.10 (0.83-1.44); .513
Previous heart disease	1.07 (0.88-1.30); .514	-
Haematologist control	1.34 (1.10-1.65); .004	1.35 (1.09-1.66); .005
Diabetes mellitus	1.39 (1.12-1.73); .003	1.23 (0.94-1.61); .124
Charlson Index	1.14 (1.05-1.24); .003	1.08 (0.96-1.21); .203
Previous bleeding	1.58 (0.87-2.84); .131	1.26 (0.68-2.31); .463
$CHADS_2$ score	1.11 (1.03-1.21); .008	0.95 (0.78-1.15); .587
CHA_2DS_2-VASc score	1.09 (1.02-1.16); .007	1.03 (0.89-1.19); .720
HAS-BLED score	1.18 (1.07-1.30); .001	1.12 (0.98-1.27); .095

OR, odds ratio; CI, confidence interval.

4. DISCUSSION

The results of this ancillary study from the FANTASIIA Registry show that 60% AF patients had poor quality control with VKA therapy (ie TTR <70%), with a slightly better management of anticoagulation by GPs. Poor anticoagulation control was evident in patients with AF, although the management of anticoagulation by GPs was slightly better.

Previous studies have shown that poor anticoagulation control is associated with a worse prognosis, increasing not only the risk of stroke and systemic embolism, but also increasing bleeding, ischaemic heart disease and mortality.[11, 19-22] In clinical practice, the TTR levels are below than those reported in randomised trials where fewer confounding variables exist and strict criteria for patient selection prevail. The GARFIELD-AF registry[20] showed an increased risk of 2.6 for thromboembolism, 1.5-fold high risk for bleeding and all-cause mortality of 2.5 with TTR <65%.

Clinical guidelines recommend the evaluation of TTR using Rosendaal method and its use should alert healthcare practitioners to inadequate anticoagulation control. However, the use of this method in daily clinical practice is difficult and in this sense, the availability of instruments that facilitate the use of Rosendaal, perhaps incorporated automatically in the electronic history and elements such as electronic alerts, could be elements of improvement.

This comparative analysis between two varying organisational models is reflected in the international literature but poorly established, at least as far as we know, in the current literature in our country, which describes results separately depending on GPs or haematologists. For this reason, the FANTASIIA Registry provides an ideal scenario to study this topic. In our series, patients with anticoagulation control by GPs represent greater than 50%. Mean age, percentage of

women, type of AF, comorbidies, risk factors, stroke and previous major bleeding were similar in both populations, although in the haematologist-controlled group, there was greater concomitant use of antiplatelet agents. In addition, patients in both groups were at high risk of both thrombotic and haemorrhagic events, similar to the GARFIELD-AF registry data.[20] Nevertheless, patients with anticoagulation control by GPs had significantly more concomitant cardiac and extracardiac pathology. Many patients in this group were clinically followed by cardiologists and consistent with the literature,[23, 24] a strategy of control of rhythm control, cardioversion and previous ablation was decided in a greater proportion of patients in comparison with those in which the control of anticoagulation was performed by haematologists with less clinical follow-up by cardiologists.

Differences in TTR and quality of anticoagulation control have been reported previously between patients controlled by GPs with those controlled by haematologic clinics. In a meta-analysis by Baker et al,[25] 8 studies with more than 22 000 patients demonstrated a mean TTR of 55%, being significantly lower when the control was carried out by GPs vs Hematology (63 vs 51%). In our study, the mean TTR estimated by the Rosendaal method had higher values than in the American study. In contrast, mean TTR in our analysis was significantly higher in patients controlled by GPs than by haematologists. In addition, the higher propensity towards poorer control associated with being the haematologist responsible for control of anticoagulation was not modified when the analyses were adjusted for the variables associated with poor control of anticoagulation such as a high HAS-BLED score or history of bleeding. It should be noted that we are not comparing professionals (haematologist vs primary care physicians) but two differing anticoagulation management systems (including number of visits, patient accessibility and availability of important clinical information). However, there are other models to assess the quality of anticoagulation. Hou et al$_{26}$ performed a systematic review of 8 clinical trials and 9 observational studies and observed that the risk of thromboembolic and bleeding events significantly decreased in patients where the anticoagulation management was based on pharmacist-led management compared to the anticoagulation clinics or treatment with GPs. Conversely, many studies have reported improvements in the quality of oral anticoagulation with self-testing and self-management approaches, with possible improvements in clinical outcomes. Verret et al[27] demonstrated that self-management of anticoagulation in AF patients improved the quality of life with the same or higher quality of anticoagulation compared to the management in anticoagulation clinics. These results reflect different models focus on the importance of the patient as an active actor of the decision-making process of anticoagulation therapy. In this way, it is mandatory to facilitate the access to the anticoagulation control. GPs generally are closer to AF patient's homes than anticoagulation clinics. Indeed, some studies reflect the efficacy of point-of-care testing devices with CoaguChek® to avoid wasting a lot of time performing blood sample test in the anticoagulation clinics.[28]

Nevertheless, in our study, the TTR levels reflected a poor quality of anticoagulation with VKAs, independent of the specialist in charge. These data contrast with the Swedish registry AuriculA[29] that included more than 18 000 patients and showed a high rate of good quality of the anticoagulation and a mean TTR of 76%, and better still in primary care with TTR of 80% than in the haematology clinics with mean TTR of 76%. The authors argued that this difference could be because the population controlled by GPs could be healthier, with less comorbidity and difficulty in maintaining the INR in range. This is not the case in this present study, where the population controlled in primary care had a slightly better quality of anticoagulation although they had more previous heart disease, lower left ventricular ejection fraction and worse renal function. Most likely, the cause of this difference in our study is related to the different organisational systems.

In any case, we observed a low TTR, independent of the anticoagulation management specialist. Also, several studies[19, 30-33] showed that 40%-54% of anticoagulated patients with VKAs in our country had a low quality of anticoagulation with a TTR of <65% estimated by Rosendaal. Additionally, the different organisational models of anticoagulation control should be aimed at improving quality. Centralised control, without direct patient review, has not been shown in our study to lead to improvement.

The results of our analysis of the FANTASIIA registry, like the data from previous studies, show that there is wide room for improvement of anticoagulation control and prognosis of patients in daily clinical practice. This makes it necessary to optimize treatment with all available variables, such as the correct training of professionals, the homogenous management of AF by the different specialists involved, the training of patients and the accessibility of direct anticoagulants that have the same or better effectiveness than warfarin with better safety profile1 The design of the FANTASIIA Registry offers the possibility to know this improvement, with the further analysis planned for 1 year, two and 2 years of evolution.

4.1 Limitations

We are comparing two systems that differ not only in professionals involved but also in different variables of difficult weight such as number of visits and determinations, availability of relevant clinical information or hospital admissions, but we had available 12 values of the INRs of each patient. In this analysis, the number of patients included, the dispersion of the participants and the selection of the patients indicate that the information provided is a good approximation of the quality of AVK anticoagulation in Spain with different organisational systems.

5. CONCLUSIONS

In the FANTASIIA registry, about 60% of AF patients anticoagulated with VKAs had poor anticoagulation control and their management was only slightly better than when the management was performed by general practitioners. Overall, there is wide room for improvement in anticoagulation quality and it seems that anticoagulation control focused on primary care is only slightly better.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

REFERENCES

1. Kirchhof P, Benuss S, Kotecha D, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J*. 2016;37:2893-2962.
2. January CT, Wann LS, Alpert JS, 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. *Circulation*. 2014;130:199-267.
3. Gómez-Doblas JJ, Muñiz J, Alonso Martin JJ, et al. Prevalencia de fibrilación auricular en España. Resultados del estudio OFRECE. *Rev Esp Cardiol*. 2014;67:259-269.
4. Miller PS, Andersson FL, Kalra L. Are cost benefits of anticoagulation for stroke prevention in atrial fibrillation underestimated? *Stroke*. 2005;36:360-365.
5. Wang TJ, Larson MG, Levy D, et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. *Circulation*. 2003;107:2920-2925.
6. Krahn AD, Manfreda J, Tate RB, et al. The natural history of atrial fibrillation: incidence, risk factors, and prognosis in the Manitoba Follow-Up Study. *Am J Med*. 1995;98:476-484.
7. Stewart S, Hart CL, Hole DJ, et al. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. *Am J Med*. 2002;113:359-364.
8. Kirchchof P, Ammentorp B, Darius H, De Caterina R, et al. Management of atrial fibrillation in seven European countries after the publication of the 2010 ESC Guidelines on atrial fibrillation: primary results of the PREFER in AF. *Europace*. 2014;16:6-14.

9. Lip GYH, Laroche C, Dan GA, et al. A prospective survey in European Society of Cardiology member countries of atrial fibrillation management: baseline results of EORP-AF Pilot General Registry. *Europace*. 2014;16:308-319.
10. Lip GYH, Laroche C, Ioachim PM, et al. Prognosis and treatment of atrial fibrillation patients by european cardiologists: one year follow-up of the EORP-AF Pilot registry. *Eur Heart J*. 2014;35:3365-3376.
11. Connolly SJ, Pogue J, Eikelboom J, et al. Benefit of oral anticoagulant over antiplatelet therapy in atrial fibrillation depends on the quality of International normalized ratio control achieved by centres and countries as measured by time in therapeutic range. *Circulation*. 2008;118:2029-2037.
12. Chan PH, Li WH, Hai JJ, et al. Time in therapeutic range and percentage of international normalized ratio in the therapeutic range as a measure of quality of anticoagulation control in patients with atrial fibrillation. *Can J Cardiol*. 2016;32:1247. e23–1247.e28.
13. Rosendaal FR, Cannegieter SC, van der Meer FJ, Briet E. A method to determine the optimal intensity of oral anticoagulant therapy. *Thromb Haemost*. 1993;69:236-239.
14. Björck F, Renlund H, Lip GYH, Wester P, Svensson PJ, Själander A. Outcomes in a Warfarin-treated population with atrial fibrillation. *JAMA Cardiol*. 2016;1:172-180.
15. Sjögren V, Grzymala-Lubanski B, Renlund H, et al. Safety and efficacy of well managed warfarin. A report from the Swedish quality register Auricula. *Thromb Haemost*. 2015;113:1370-1377.
16. Roldán Rabadán I, Anguita Sánchez M, Marín F, et al. Tratamiento antiarrítmico actual de la fibrilación auricular no valvular en España. Datos del Registro FANTASIIA. *Rev Esp Cardiol*. 2016;69:54-60.
17. Simera I, Moher D, Hoey J, Schulz KF, Altman DG. A catalogue of reporting guidelines for health research. *Eur J Clin Invest*. 2010;40:35-53.
18. Fihn SD, McDonell M, Martin D, et al. Risk factors for complications of chronic anticoagulation. A multicenter study. Warfarin optimized outpatient follow-up study group. *Ann Intern Med*. 1993;118:511-520.
19. Bertomeu-González V, Anguita M, Moreno-Arribas J, et al. Quality of anticoagulation with vitamin K antagonists. *Clin Cardiol*. 2015;38:357-364.
20. Haas S, Ten Cate H, Accetta G, et al. Quality of vitamin K antagonist control and 1-year outcomes in patients with atrial fibrillation: a global perspective from the GARFIELD-AF registry. *PLoS ONE*. 2016;11:e0164076.
21. Morgan CL, McEwan P, Tukiendorf A, et al. Warfarin treatment in patients with atrial fibrillation: observing outcomes associated with varying levels of INR control. *Thromb Res*. 2009;124:37-41.
22. Pastori D, Pignatelli P, Saliola M, et al. Inadequate anticoagulation by Vitamin K antagonists is associated with Major Adverse Cardiovascular Events in patients with atrial fibrillation. *Int J Cardiol*. 2015;15:513-516.
23. Fosbol EL, Holmes DN, Piccini JP, et al. Provider specialty and atrial fibrillation treatment strategies in United States community practice: findings from the ORBIT-AF registry. *J Am Heart Assoc*. 2013;2:e000110.
24. Funk AM, Kocher KE, Rohde JM, et al. Variation in practice patterns among specialties in the acute Management of atrial fibrillation. *BMC Cardiovasc Disord*. 2015;15:21.
25. Baker WL, Cios DA, Sander SD, Coleman CI. Meta-analysis to assess the quality of warfarin control in atrial fibrillation patients in the United States. *J Manag Care Pharm*. 2009;15:244-252.
26. Hou K, Yang H, Ye Z, Wang Y, Liu L, Cui X. Effectiveness of pharmacist-led anticoagulation management on clinical outcomes: a systematic review and meta-analysis. *J Pharm Pharm Sci*. 2017;20:378-396.
27. Verret L, Couturier J, Rozon A, et al. Impact of a pharmacist-led warfarin self-management program on quality of life and anticoagulation control: a randomized trial. *Pharmacotherapy*. 2012;32:871-879.
28. Okuyama Y, Matsuo M, Matsuo H, et al. Introduction of point-of-care testing in Japanese outpatient clinics is associated with improvement in time in therapeutic range in anticoagulant-treated patients. *Circ J*. 2014;78:1342-1348.
29. Wieloch M, Själander A, Frykman V, et al. Anticoagulation control in Sweden: reports of time in therapeutic range, major bleeding, and thrombo-embolic complications from the national quality registry AuriculA. *Eur Heart J*. 2011;32:2282-2289.
30. Anguita M, Cequier A, Bertomeu V; e Investigadores del Estudio CALIFA. Mal control de la anticoagulación con antagonistas de la vitamina K en pacientes con fibrilación auricular no valvular en España: prevalencia actual y factores asociados. *Rev Esp Cardiol* 2015; 68:761-768.

31. Barrios V, Escobar C, Prieto L, et al. Anticoagulation control in patients with nonvalvular atrial fibrillation attended at primary care centres in Spain: the PAULA Study. *Rev Esp Cardiol*. 2015;68:769-776.
32. Sinza-Sanjurjo S, Rey-Aldana D, Gestal-Pereira E, Calvo-Gómez C. Evaluación del grado de anticoagulación de pacientes con fibrilación auricular en el ámbito de atención primaria en Galicia. Estudio ANFAGAL. *Rev Esp Cardiol*. 2015;68:753-760.
33. Hugo GS, Figueiras-Graillet LM, Anguita M, et al. Oral anticoagulation in octogenarians with atrial fibrillation. *Int J Cardiol*. 2016;223:87-90.