Contents available at **PubMed**
www.clinicalandtranslationalinvestigation.com

Check for updates

ORIGINAL ARTICLE

Impact on Adherence and Clinical Outcomes of an Anticoagulation Stewardship Program in Users of Direct Oral Anticoagulants

Mayra A. Arenas-Beltrán[1*], Paula Ruiz-Talero[1,2], Karen Navarro-Pérez[1,2], Pilar Alarcón-Robles[1,2], Alice Daniela.Salamanca[3], and Oscar M. Muñoz-Velandia[1,2]

[1]Department of Internal Medicine, Faculty of Medicine, Pontificia Universidad Javeriana, Bogotá, Colombia; [2]Department of Internal Medicine, Hospital Universitario San Ignacio, Bogotá, Colombia; [3]Nursing Department, Hospital Universitario San Ignacio, Bogotá, Colombia

ABSTRACT

Background: Anticoagulation stewardship in warfarin users reduces thromboembolic and bleeding events and improves adherence. Limited data exist on its impact on adherence among direct oral anticoagulants (DOACs) users. **Objective:** To evaluate whether inpatient and outpatient follow-up in an anticoagulation stewardship program improves adherence and clinical outcomes in DOAC users compared to usual care. **Methods:** Cohort study of patients initiating DOAC therapy at a university medical center. Participants were categorized into anticoagulation stewardship and usual care cohorts. Adherence was assessed at 30, 90, and 180 days. Univariate and multivariate logistic regression models were used to identify factors associated with lower adherence. **Results:** 250 patients were included, with 81 receiving anticoagulation stewardship follow up. Adherence at 30 days was intermediate-high in over 90% of participants. The no-follow-up group showed a higher proportion of patients with low adherence (9.4% versus 2.4%, p = 0.003) and bleeding complications (4.1% versus 0%, p = 0.063). Anticoagulation stewardship exhibited a trend toward higher adherence (odds ratio [OR]: 3.51; 95% confidence interval [CI]: 0.74–16.47; p = 0.107). Factors associated with lower adherence included higher educational level (OR: 0.20; 95% CI: 0.05-0.75; p = 0.018), enrollment in a subsidized health system (OR: 0.08; 95% CI: 0.01-0.64; p = 0.018), and deep venous thrombosis as an indication for anticoagulation. **Conclusion:** Anticoagulation stewardship programs may enhance adherence to DOAC therapy. Prospective studies are needed to confirm these findings. (REV INVEST CLIN. 2025;77(2):44-54)

Keywords: Anticoagulation stewardship. Drug adherence. Direct-acting oral anticoagulant. Atrial fibrillation. Venous thromboembolism.

*Corresponding author:
Mayra A. Arenas-Beltrán
E-mail: mayra.arenas@javeriana.edu.co

INTRODUCTION

Venous thromboembolism (VTE) and atrial fibrillation (AF) are the major indications for anticoagulant therapy worldwide. VTE is a common entity with an incidence in Europe and the United States of 1-2 cases/1000 person-years, increasing with age, cancer diagnosis, and being more frequent in women in childbearing age and in men over 45 years of age; the mortality is up to 20% in the 1st year after the thrombotic event[1,2]. In Latin America, the reported incidence is approximately 0.7 cases/1000 person-years, with a mortality of 5% for pulmonary thromboembolism and 3.4% for deep vein thrombosis (DVT)[3]. AF is a pathology with an increasing incidence, directly related to age, and with a prevalence of 30.3 cases/100,000 people worldwide; it is estimated that one in five people over the age of 45 will be diagnosed with this entity, whose main complication is a 4-5-fold increase in the risk of stroke[4,5].

Direct oral anticoagulants (DOACs) are the treatment of choice for VTE and AF, with evidence of an 85% reduction in the risk of recurrent VTE, a 15% reduction in ischemic stroke and systemic embolic events compared with warfarin, and an 11% reduction in all-cause mortality in patients with AF[6-8]. DOACs are also safer, causing a 48% reduction in major bleeding events compared with vitamin K antagonists[8]. Poor adherence to DOACs is associated with an increase in all-cause mortality (HR = 1.54) and a 40% increase in the risk of ischemic stroke in patients with AF[9,10].

Since the 1990s, systematic management and coordinated monitoring of oral and parenteral anticoagulants have been shown to improve clinical outcomes[11]. Initially, there were clinics for patients anticoagulated with warfarin, which demonstrated a 31% reduction in the incidence of thromboembolic events, bleeding, and all-cause mortality compared to usual care, as well as up to 7% increase in the time in therapeutic range[12,13]. In the case of DOACs, the focus is different because frequent dose adjustments are not required, so the activities of these programs focus on monitoring renal and hepatic function, confirmation of indication, dose adjustments, and education on drug use to promote adherence. These strategies have been shown to increase the correct prescribed dose to 93% and reduce the rate of major bleeding by up to 43%[14,15]. Pharmacist-led and telephone feedback strategies are known to increase correct dispensing to 91%, and adherence expressed as the proportion of days covered; however, the impact of multidisciplinary follow-up strategies on adherence in patients using DOACs is not clear[16,17]. More recently, the concept of anticoagulation stewardship has emerged, which refers to system-level initiatives aimed at optimizing anticoagulant-related health outcomes and minimizing adverse events through evidence-based care, appropriate use of anticoagulants, and effective patient monitoring[11,18].

The aim of this study was to evaluate whether inpatient and outpatient follow-up within an anticoagulation stewardship program improves adherence and clinical outcomes in DOAC users compared to usual care, after controlling for multiple confounding variables, based on the experience of a Latin American program.

METHODS

Study design and participants

This observational, analytical cohort study included patients aged ≥ 18 years who initiated DOAC therapy (apixaban, rivaroxaban, and dabigatran) during hospitalization for AF, VTE, or other indications (e.g., left ventricular thrombus) at Hospital Universitario San Ignacio in Bogota, Colombia, between February 2022 and August 2024. Patients were identified through the Hospital Universitario San Ignacio's institutional anticoagulation registry (RAC-HUSI). This institutional registry includes all patients starting anticoagulant therapy for any diagnosis at the hospital. Patients who were followed in anticoagulation clinics of other institutions, those who died during hospitalization, and those who did not have at least one telephone contact for the registry follow-up were excluded from the study. The study was approved by the Ethics and Research Committee of the Hospital Universitario San Ignacio (FM-CIE-0420-23).

The RAC-HUSI is an institutional registry that collects demographic and clinical information on all patients starting anticoagulant therapy in the hospital. Information is systematically collected at the point of care using standardized tools. All patients in the registry have telephonic follow-up at 30, 90 and 180 days after discharge. This registry follow-up is independent

of the anticoagulation stewardship program. The REDCap (Research Electronic Data Capture) tools, hosted at the Hospital Universitario San Ignacio, were used to collect and manage the information[19,20]. Sociodemographic variables (age, socioeconomic status, occupation, health system, and education), comorbidities for the calculation of the Charlson index (Table S1), and number of medications were obtained from the institutional anticoagulation registry. Regular audits of the data collection process were performed to identify areas for improvement and to ensure data quality. Where missing information was identified, it was supplemented by a retrospective review of institutional electronic medical records. Each patient included in the registry was followed up by telephone calls at 30, 90, and 180 days after discharge by a trained nurse. The nurse used a predefined interview format in RedCap that included the 8-factor Morisky Green questionnaire (MMAS-8) for evaluating adherence and the patient's report of thrombotic or hemorrhagic events.

The Morisky-Green 8-factor questionnaire (MMAS-8) (Table S2) was used to assess adherence, with scores ranging from 0 to 8 points. Patients were classified into three categories based on their adherence score: high adherence (score of 6 to < 8 points), and low adherence (score < 6 points). For the analysis, adherence was dichotomized as non-adherent (score < 6) or adherent if the score was greater or equal to 6 (i.e., intermediate and high categories of the MMAS-8)[21].

Our hospital has implemented since 2020 an Anticoagulation Stewardship model, based on the core elements suggested by the Anticoagulation Forum[18]. This model includes activities that are common for all the hospital, like evidence – based clinical practice guidelines and continued medical education, and other activities that are related to an inpatient consultation with the anticoagulation clinic. In this consultation, patients are evaluated by internal medicine physicians with special training in thrombosis and anticoagulation; they receive patient education sessions with nurses and ensure a safe transition of care by offering a follow-up consultation after hospitalization in the outpatient setting. Patients included in the analysis were divided into two groups. One group was termed "anticoagulation stewardship program follow-up" and included patients who underwent in-hospital evaluation by the medical team of the institutional

anticoagulation clinic, received education on the use of DOACs from nurses during their hospital stay, and had at least one follow-up visit to the program's outpatient clinic. The second cohort, referred to as "no follow-up in the anticoagulation stewardship program," consisted of patients who did not meet the criteria for enrollment in the follow-up cohort and received usual care.

The activities of the anticoagulation stewardship program were independent of the institutional anticoagulation registry, so although a group of patients were not followed up by the anticoagulation stewardship program, patients in both groups were included in the institutional anticoagulation registry (RAC-HUSI), so they had the same systematic telephone monitoring to assess adverse events (thrombotic and hemorrhagic) and the adherence measurement strategy mentioned above, performed by a trained nurse who was unaware of the patient group assignment.

Bleeding events were classified according to the definitions proposed by the International Society on Thrombosis and Haemostasis (ISTH)[22]. Major bleeding was defined as bleeding that met one of the following criteria: fatal bleeding, bleeding at a critical site, bleeding associated with hemodynamic instability, or bleeding resulting in a decrease of 2 g of hemoglobin or requiring transfusion of 2 or more units of red blood cells. Non-major bleeding was defined as bleeding that did not meet the criteria for major bleeding. A thrombotic event was defined as imaging evidence (Doppler, tomography, magnetic resonance, or perfusion ventilation scintigraphy) of pulmonary embolism, DVT, thrombosis in an unusual site, stroke, or transient ischemic attack reported by the patient during telephone follow-up or documented in the institutional medical history.

The sample size was calculated to detect a difference in the proportion of patients adhering to treatment that would increase from 60% in patients without anticoagulation stewardship program follow-up to 76% in patients with anticoagulation stewardship program follow-up. These calculations were made using an alpha error of 0.05% and 80% power for a 2-tailed hypothesis. The calculated sample size was determined to be 266 patients, with 133 patients assigned to each group.

Figure 1. Flow diagram of patients included in the analysis.
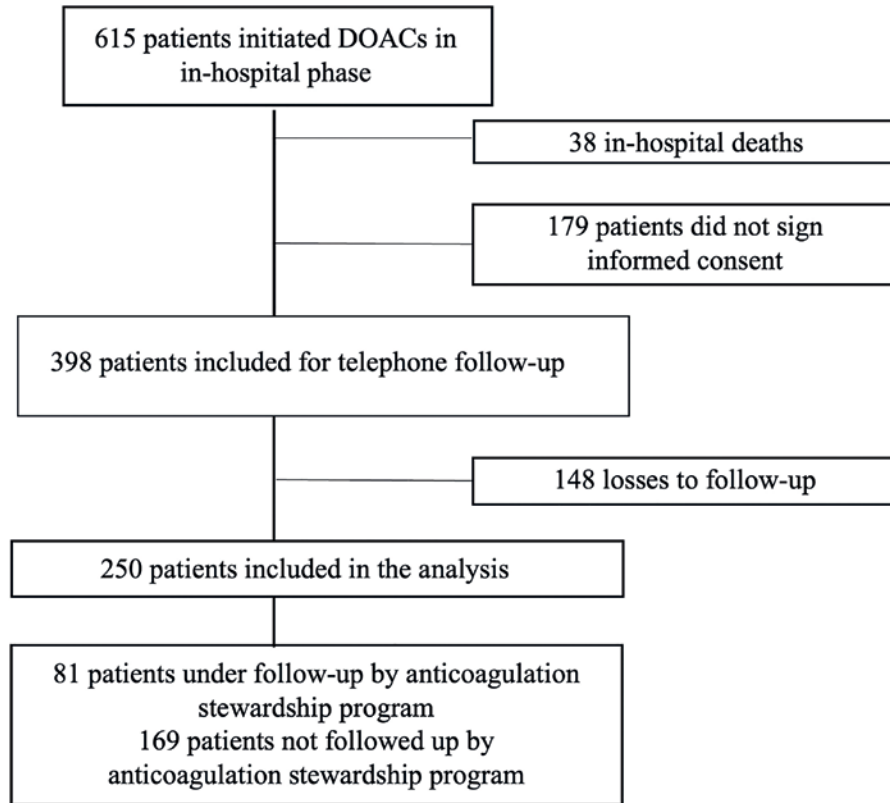
Statistical analysis

Absolute and relative frequencies were used to describe qualitative variables. Measures of central tendency and dispersion were calculated for quantitative variables, mean and standard deviation for variables with normal distribution, and median with interquartile range for variables with non-normal distribution. The Shapiro-Wilk test was used to assess the normality assumption. Categorical variables are presented as absolute numbers and percentages. Comparisons between groups were made using a t-test, Mann-Whitney U test, or χ^2 test, depending on the characteristics of the variables. To evaluate the association between anticoagulation stewardship program participation and adherence, we used a logistic regression model. We first performed a univariate analysis and then a multivariate analysis adjusting for factors with a significant association in the univariate analysis. The Backward Stepwise method was used to identify independently associated variables. Statistical analysis was performed using STATA software version 16 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC).

RESULTS

Of the 615 patients who initiated anticoagulation with DOACs, 398 met the study inclusion criteria and 250 were ultimately included in the analysis (81 were followed up by the anticoagulation stewardship program and 169 were not followed up). The selection process is shown in figure 1. The clinical and sociodemographic characteristics of the analyzed patients are described in table 1. Patients in the anticoagulation stewardship program were younger (67 versus 73 years, p = 0.005) and had better renal function (eGFR 86 versus 72 mL/min/1.73 m³, p = 0.003). The primary indication for anticoagulation was pulmonary embolism, which was observed to be more prevalent in patients enrolled in the anticoagulation stewardship program (56.7% versus 33.1%, p ≤ 0.001). The remaining characteristics showed no significant differences between the two groups.

Table 1. Demographic and clinical characteristics of patients according to anticoagulation stewardship program follow-up

Variable	No follow-up in anticoagulation stewardship program (n = 169)	Anticoagulation stewardship program follow-up (n = 81)	p
Age, years, median (RIQ)	73 (62-80)	67 (56-74)	0.005
Female sex, n (%)	73 (43.2)	38 (46.9)	0.580
Job occupation, n (%)	45 (26.6)	30 (37)	0.093
Contributive health care system, n (%)	162 (95.8)	80 (98.7)	0.222
Socioeconomic stratum, n (%)			0.862
1	23 (13.6)	10 (12.3)	
2	74 (43.7)	37 (45.6)	
3	52 (36.6)	29 (35.8)	
4	8 (4.7)	5 (6.1)	
5	2 (1.1)	0 (0)	
Secondary or higher education level, n (%)	77 (45.5)	45 (55.5)	0.139
Indication for anticoagulation, n (%)			< 0.001
PE	56 (33.1)	46 (56.7)	
DVT	54 (31.9)	19 (23.4)	
Atrial Fibrillation/Flutter	59 (34.9)	13 (16)	
Other	0 (0)	3 (3.7)	
Charlson index, n (%)			0.320
Absence of comorbidity	26 (15.3)	11 (13.5)	
Low comorbidity	41 (24.1)	27 (33.3)	
High comorbidity	102 (60.3)	43 (53)	
HAS-BLED, n (%)			0.461
Low risk	159 (94)	78 (96.3)	
High risk	10 (5.9)	3 (3.7)	
Polypharmacy, n (%)	102 (60.3)	49 (60.4)	0.983
Use of antiplatelet drugs	25 (14.9)	8 (9.8)	0.282
eGFR, mL/min/m³, median (RIQ)	72 (52-94.5)	86 (64-104)	0.003
Cirrhosis Child-Pugh B, n (%)	3 (1.7)	3 (3.7)	0.351

PE: pulmonary embolism; DVT: deep vein thrombosis; eGFR: estimated glomerular filtration rate.

Adherence at 30 days was intermediate-high in more than 90% of patients in both groups, with a higher percentage of patients with low adherence among those who were not followed up by the anticoagulation stewardship program (9.4% versus 2.4%, p = 0.003). Hemorrhagic events were observed exclusively in the non-follow-up group (4.1% versus 0%, p = 0.063). All hemorrhagic events were non-major and included hematuria and abnormal uterine bleeding. A single thrombotic event, corresponding to a stroke, was documented in the group that was not followed up by the anticoagulation stewardship program. The frequencies of the outcomes of interest are shown in table 2.

Table 3 shows the factors associated with optimal adherence. In univariate analysis, participation in an anticoagulation stewardship program showed a trend

Table 2. Frequency of adherence and thrombotic and hemorrhagic events according to anticoagulation stewardship program follow-up

Variable	No follow-up in anticoagulation stewardship program (n = 169)	Anticoagulation stewardship program follow-up (n = 81)	p
Adherence at 30 days, n (%)			
Intermediate-high	153 (90.5)	79 (97.5)	0.003
Low	16 (9.4)	2 (2.4)	
Thrombotic events, n (%)	1 (0.59)	0 (0)	0.488
Hemorrhagic events, n (%)	7 (4.1)	0 (0)	0.063

Table 3. Univariate and multivariate analysis to evaluate the importance of follow-up in an anticoagulation stewardship program as a factor associated with 30-day adherence in patients on anticoagulation with DOACs

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Anticoagulation stewardship follow-up	4.13 (0.92-18.41)	0.063	3.51 (0.74-16.47)	0.107
Age	1.02 (0.99-1.05)	0.122		
Sex	1.27 (0.48-3.32)	0.620		
Occupation	1.97 (0.74-5.20)	0.172		
Secondary education level or higher	0.34 (0.11-0.98)	0.047	0.20 (0.05-0.75)	0.018
Subsidized health system	0.21 (0.39-1.13)	0.070	0.08 (0.01-0.64)	0.017
Socioeconomic stratum				
2	1.01 (0.26-3.90)	0.261		
3	1.71 (0.38-7.63)	0.387		
Indication for anticoagulation				0.037
PE	Reference		Reference	
DVT	0.19 (0.50-0.72)	0.015		
Atrial fibrillation	0.40 (0.93-1.75)	0.228	0.23 (0.05-0.91)	
eGFR				
< 60 mL/min^3	0.64 (0.17-2.36)	0.504		
60-90 mL/min/m^3	0.5 (0.14-1.72)	0.273		
Polypharmacy	2 (0.76 -5.28)	0.157		
In-hospital consult by the Anticoagulation Clinic	2.34 (0.74-7.33)	0.144		

PE: pulmonary thromboembolism; DVT: deep vein thrombosis; eGFR: estimated glomerular filtration rate.

toward better adherence, although this did not reach statistical significance (odds ratio [OR]: 4.13; 95% confidence interval [CI]: 0.92-18.41; p = 0.063). Multivariate analysis showed a similar result (OR: 3.51; 95% CI: 0.74-16.47; p = 0.107), and a higher level of education (secondary school or higher) was identified as a factor associated with lower adherence (OR: 0.20; 95% CI: 0.05-0. 75; p = 0.018), as was having a subsidized health plan (OR: 0.08; 95% CI: 0.01-0.64; p = 0.018) or the indication for anticoagulation being DVT versus pulmonary embolism (OR: 0.23; 95% CI: 0.05-0.91; p = 0.037).

A total of 148 patients (37.1%) who initiated DOACs were lost to follow-up after 30 days. The sociodemographic and clinical characteristics of patients lost to

Table 4. Demographic and clinical characteristics of patients with DOACs according to loss to 30-day follow-up

Variable	No loss to follow-up (n = 250)	Loss to follow-up (n = 148)	p
Age, years, median (RIQ)	71 (58-79)	71.5 (60-79.5)	0.502
Female sex, n (%)	139 (55.6)	85 (57.4)	0.722
Job occupation, n (%)	75 (30)	90 (60.8)	0.060
Contributive health care system, n (%)	242 (96.8)	143 (96.6)	0.923
Socioeconomic stratum, n (%)			0.466
1	33 (13.2)	17 (11.4)	
2	111 (44.4)	64 (43.2)	
3	91 (36.4)	51 (34.4)	
4	13 (5.2)	15 (10.1)	
5	2 (0.8)	1 (0.68)	
Secondary or higher education level, n (%)	122 (48.8)	73 (49.2)	0.860
Indication for anticoagulation, n (%)			0.183
PE	102 (40.8)	45 (30.4)	
DVT	73 (29.2)	54 (36.4)	
Atrial Fibrillation/Flutter	72 (28.8)	46 (31)	
Other	3 (1.2)	3 (2)	
Charlson index, n (%)			0.594
Absence of comorbidity	37 (14.8)	24 (16.2)	
Low comorbidity	68 (27.2)	39 (26.3)	
High comorbidity	145 (58)	85 (57.4)	
HAS-BLED, n (%)			0.604
Low risk	237 (94.8)	142 (95.9)	
High risk	13 (5.2)	6 (4.0)	
Polypharmacy, n (%)	151 (60.4)	85 (57.4)	0.560
eGFR, ml/min/m^3, median (RIQ)	75 (55-96)	75 (53-97)	0.300

PE: pulmonary thromboembolism; DVT: deep vein thrombosis; eGFR: estimated glomerular filtration rate.

follow-up compared with those who remained in the study are shown in table 4. The results indicate that the two groups had similar characteristics except for a higher number of patients with a job occupation in the lost-to-follow-up group (60.8 versus 30%; p = 0.060).

There were 47 patients lost to follow-up at 90 days and an additional 41 patients lost to follow-up at 180 days. Figure 2 shows the percentage of intermediate-high adherence at 90 and 180 days. No statistically significant differences were observed between the adherent and non-adherent groups by anticoagulation stewardship program at 90 and 180 days. However, a decrease in the percentage of intermediate-high adherence was observed in both groups at 180 days.

DISCUSSION

The aim of the present study was to evaluate whether follow-up in an anticoagulation stewardship program is associated with improved adherence to

Figure 2. Percentage of adherence at 30, 90, and 180 days according to anticoagulation stewardship program follow-up.
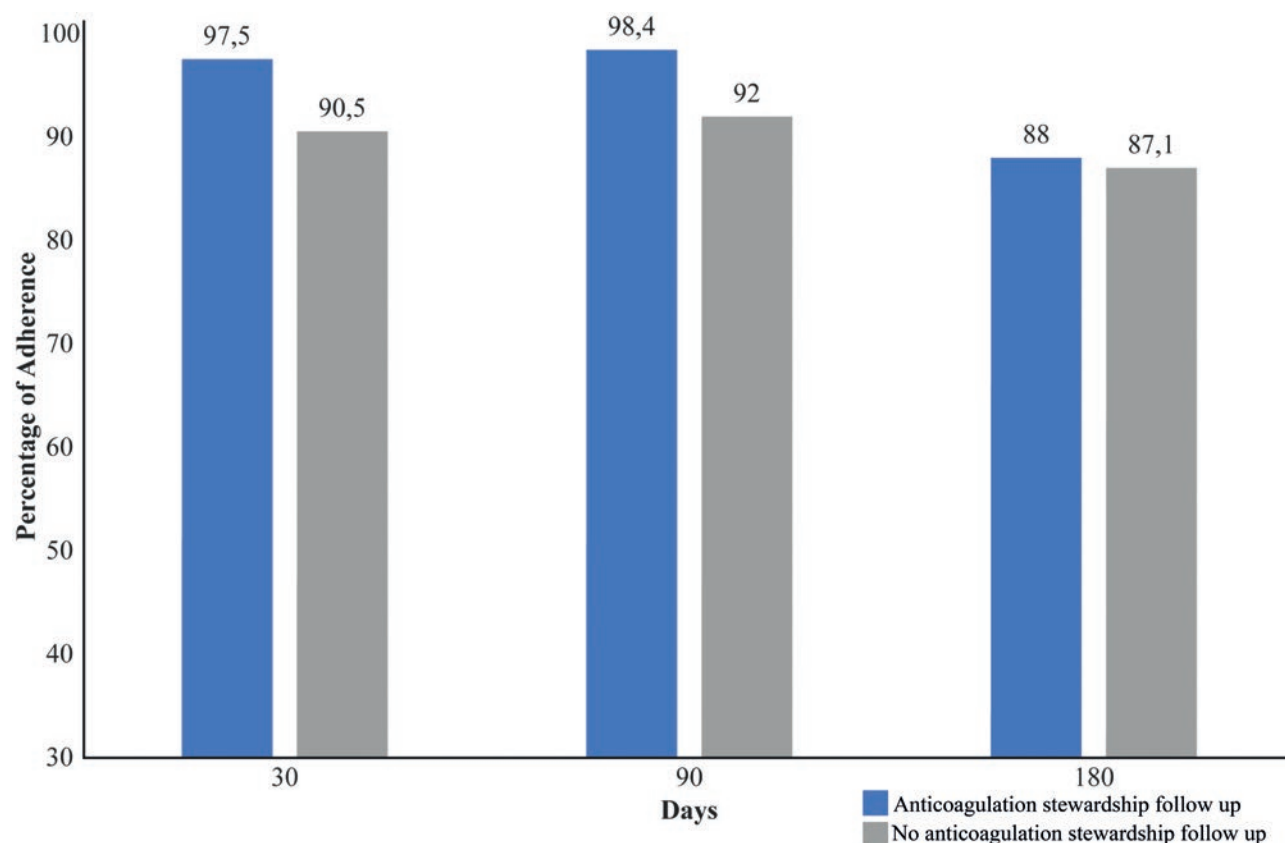
DOACs and better clinical outcomes. The results showed a trend toward improved adherence, with a concomitant reduction in bleeding and thrombosis.

Anticoagulation clinics have previously been shown to have a positive impact on warfarin users, resulting in a 31% reduction in the combined outcome of thromboembolic events, bleeding and all-cause mortality, and up to a 60% reduction in thrombotic events, with a concomitant positive effect on adherence expressed as time in therapeutic range[16,17].

In the present study, the percentage of adherent patients at 30 days was over 90% in patients with and without anticoagulation stewardship program follow-up. This rate was higher than that reported in other studies of patients with AF and VTE on DOACs therapy, in which adherence ranged from 66-90.2% as assessed by PDC (proportion of days covered), MPR (medication possession ratio), or self-reported adherence questionnaires such as

MARS-5 and MMAS-8[10,23-26]. A comparative analysis of the present results with other studies using the MMAS-8 revealed adherence levels consistent with those observed in this study. Specifically, 80-92% of patients in cohorts from the United Kingdom, Italy, and Egypt demonstrated intermediate to high adherence[23,27,28]. This is generally higher than PDC and MPR. The higher level of adherence observed in this study may be since more than 50% of the patients included in the analysis received education on anticoagulant use during hospitalization, regardless of whether or not they continued to receive follow-up care through the institutional anticoagulation stewardship program. The use of a self-report questionnaire as a method of measuring adherence, combined with assessment of adherence at 30, 90, and 180 days, as described in other studies, may have contributed to the results. A number of studies have shown that adherence tends to decrease over time, particularly after the first 6 months to 1 year of follow-up[29].

When evaluating the impact of anticoagulation stewardship on increasing adherence, a trend was observed in favor of anticoagulation stewardship and increased adherence, with an OR of 3.5 (95% CI 0.74-16.47). However, the limited number of low adherence events in the cohort reduced the precision of the estimates, which may be due to the awareness of healthcare professionals regarding the appropriate prescription of anticoagulants based on clinical practice guidelines and the information provided to patients at the time of discharge. The potential positive impact of a multidisciplinary DOACs follow-up program has been documented for other types of activities, such as pharmacist follow-up and telephone feedback from trained personnel. These activities increased adherence to 91-97% in terms of PDC, pill count, and drug delivery in cohorts of patients in the United States[16,17]. In-hospital anticoagulation stewardship interventions have been shown to increase adherence to clinical practice guidelines and appropriate prescribing of DOACs. However, more data are needed on their impact on outpatient follow-up[13-15].

In evaluating the factors associated with lower adherence, it was found that, contrary to the literature, a higher level of education was associated with lower adherence. Therefore, it will be necessary in the future to evaluate the reasons and beliefs of patients that may influence lower adherence despite a high level of education[30,31]. A notable finding was the association between subsidized health insurance coverage (social security and government-funded health insurance) and lower adherence. This phenomenon has been observed in other contexts, such as tuberculosis and HIV, and may be due to factors such as limited access to medicines, longer waiting times for medical appointments, and higher out-of-pocket expenses. In addition, individuals enrolled in the subsidized scheme often have lower incomes, a factor that has been documented in other studies to contribute to lower adherence[32-34].

Notably, when comparing by indication for anticoagulation, patients with AF and DVT were less adherent than patients with pulmonary embolism. This phenomenon may be due to a lower perception of risk in patients with these conditions. However, no studies were identified that examined the association between the indication for anticoagulation and adherence as a conditioning element.

In the present study, no major bleeding events were observed, and all non-major bleeding events (4.1%) occurred in patients not followed up by the anticoagulation stewardship program, suggesting that the interventions of this program may influence the reduction of hemorrhagic complications. There is a confounding factor that may have influenced this result; when comparing the two groups, those in the group not followed up by the anticoagulation stewardship program had a lower eGFR, a factor that has been described as an element associated with an increased incidence of clinically relevant non-major bleeding events in DOACs users; however, the highest risk has been seen in patients with eGFR < 60 mL/min, and the median eGFR in the no follow-up group was 72 mL/min[35,36].

The incidence of non-major bleeding and thrombotic complications in our study was lower than in pivotal trials such as ARISTOTLE or ROCKET AF[37,38]. It has been shown that anticoagulation stewardship interventions, such as dose adjustment of DOACs and discontinuation of drugs that increase bleeding risk, result in a reduction of major bleeding events by up to 43%[36]. Although no major bleeding events were documented in our study, the lower incidence of non-major bleeding documented in the follow-up cohort of the anticoagulation stewardship program may be explained by the implementation of these interventions as part of the clinical follow-up.

This study is among the first to evaluate the impact of follow-up in an anticoagulation stewardship program on adherence in patients using DOACs. To date, it is the first study to evaluate this outcome in a Latin American population. A limitation of the study was the small number of events (low adherence), making our sample size insufficient, which resulted in poor precision of the estimates and precluded confirmation of the potential beneficial effect of anticoagulation stewardship. Therefore, prospective multicenter studies with larger sample sizes are needed to improve the precision of the estimates. Another limitation was the 37% loss to 30-day follow-up in patients with DOAC initiation during hospitalization. However, no significant differences were observed between those who were followed up and those who were lost to follow-up, suggesting a lower risk of bias in our estimates. Among patients lost to follow-up, the only notable finding was a higher

percentage of patients with an "employed" occupation. This may be due to the impact of work schedules and availability to attend follow-up calls or controls, as previously described in other studies. However, the results of these studies have been inconsistent, and the presence and strength of this association has not been clearly established[33].

In conclusion, results of this study suggest that the range of inpatient and outpatient interventions implemented in anticoagulation stewardship programs may have a positive impact on patient adherence to DOACs therapy, while reducing the occurrence of thrombotic and bleeding complications compared with conventional care. Further research, including larger sample sizes, is needed to substantiate the potential benefits of such programs in the long-term monitoring of DOACs users.

ACKNOWLEDGMENTS

SUPPLEMENTARY DATA

Supplementary data are available at 10.24875/RIC.25000008. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

REFERENCES

1. Lutsey PL, Zakai NA. Epidemiology and prevention of venous thromboembolism. Nat Rev Cardiol. 2022;20:248-62.
2. Wendelboe AM, Raskob GE. Global burden of thrombosis: epidemiologic aspects. Circ Res. 2016;118:1340-7.
3. Ceresetto JM. Venous thromboembolism in Latin America: a review and guide to diagnosis and treatment for primary care. Clinics (Sao Paulo). 2016;71:36-46.
4. Kornej J, Börschel CS, Benjamin EJ, Schnabel RB. Epidemiology of atrial fibrillation in the 21st century: novel methods and new insights. Circ Res. 2020;127:4-20.
5. Linz D, Gawalko M, Betz K, Hendriks JM, Lip GY, Vinter N, et al. Atrial fibrillation: epidemiology, screening and digital health. Lancet Reg Health Eur. 2024;37:100786.
6. Castellucci LA, Cameron C, Le Gal G, Rodger MA, Coyle D, Wells PS, et al. Efficacy and safety outcomes of oral anticoagulants and antiplatelet drugs in the secondary prevention of venous thromboembolism: systematic review and network meta-analysis. BMJ. 2013;347:f5133.
7. Saraiva JF. Stroke prevention with oral anticoagulants: summary of the evidence and efficacy measures as an aid to treatment choices. Cardiol Ther. 2018;7:15-24.
8. Chan YH, See LC, Tu HT, Yeh YH, Chang SH, Wu LS, et al. Efficacy and safety of apixaban, dabigatran, rivaroxaban, and warfarin in Asians with nonvalvular atrial fibrillation. J Am Heart Assoc. 2018;7:e008150.
9. Borne RT, O'Donnell C, Turakhia MP, Varosy PD, Jackevicius CA, Marzec LN, et al. Adherence and outcomes to direct oral anticoagulants among patients with atrial fibrillation: findings from the veterans health administration. BMC Cardiovasc Disord. 2017;17:236.
10. Ozaki AF, Choi AS, Le QT, Ko DT, Han JK, Park SS, et al. Real-world adherence and persistence to direct oral anticoagulants in patients with atrial fibrillation: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes. 2020;13:e005969.
11. Burnett A, Rudd KM, Triller D. Advancing anticoagulation stewardship: a call to action for stewardship from the US-based anticoagulation forum. Thromb Update. 2022;9:100125.
12. Daniels PR, Manning DM, Moriarty JP, Bingener-Casey J, Ou NN, O'Meara JG, et al. Improving inpatient warfarin therapy safety using a pharmacist-managed protocol. BMJ Open Qual. 2018; 7:e000290.
13. Eggebrecht L, Ludolph P, Göbel S, Panova-Noeva M, Arnold N, Nagler M, et al. Cost saving analysis of specialized, eHealth-based management of patients receiving oral anticoagulation therapy: results from the thrombEVAL study. Sci Rep. 2021; 11:2577.
14. Willeford A, Leiman V, Noel ZR. Impact of a pharmacist-to-dose direct oral anticoagulant protocol on medication errors at an academic medical center. J Am Coll Clin Pharm. 2021;4:1392-400.
15. Miele C, Taylor M, Shah A. Assessment of direct oral anticoagulant prescribing and monitoring pre- and post-implementation of a pharmacy protocol at a community teaching hospital. Hosp Pharm. 2017;52:207-13.
16. Navin SF, Nardolillo J, Stambaugh A, Young C, Nguyen P, Apodaca M. Pharmacist monitoring of direct oral anticoagulants for American Indians and Alaska Natives in the outpatient setting. J Am Pharm Assoc (2003). 2022;62:598-603.
17. Desteghe L, Vijgen J, Koopman P, Dilling-Boer D, Schurmans J, Dendale P, et al. Telemonitoring-based feedback improves adherence to non-vitamin K antagonist oral anticoagulants intake in patients with atrial fibrillation. Eur Heart J. 2018;39:1394-403.
18. Kaatz S, Ansell J, Burnett A, Deitelzweig S, Witt DM, Garcia D, et al. Core Elements of Anticoagulation Stewardship Programs Contributors Anticoagulation Forum Steering Committee Members Chief Executive Officer National Blood Clot Alliance. United States: Anticoagulation Forum; 2019. p. 1-40.
19. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42:377-81.
20. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: building an international community of software platform partners. J Biomed Inform. 2019; 95:103208.
21. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypert (Grennwich). 2008;10:348-54.
22. Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. J Thromb Haemost. 2005;3:692-4.
23. Brízido C, Ferreira AM, Lopes P, Strong C, Sá Mendes G, Fernandes Gama F, et al. Medication adherence to direct anticoagulants in patients with non-valvular atrial fibrillation - a real world analysis. Rev Port Cardiol (English Ed). 2021;40:669-75.
24. Salmasi S, Loewen PS, Tandun R, Andrade JG, De Vera MA. Adherence to oral anticoagulants among patients with atrial fibrillation: a systematic review and meta-analysis of observational studies. BMJ Open. 2020;10:e034778.
25. Grymonprez M, Capiau A, Steurbaut S, Mehuys E, Boussery K, De Backer TL, et al. Adherence and persistence to oral anticoagulants in patients with atrial fibrillation: a Belgian nationwide cohort study. Front Cardiovasc Med. 2022;9:994085.
26. Moudallel S, Van Laere S, Cornu P, Dupont A, Steurbaut S. Assessment of adherence, treatment satisfaction and knowledge of direct oral anticoagulants in atrial fibrillation patients. Br J Clin Pharmacol. 2022;88:2419-29.

27. Mohammed Hashem Elkerdawy N, Gomaa Ahmed N, Mohamed Khorais A. Knowledge and adherence to oral anticoagulant therapy in patients with atrial fibrillation. Egypt J Health Care. 2022;13:873-87.

28. Barcellona D, Mameli A, Cornacchini S, Perra F, Diovaldi M, Farci N, et al. Patients' adherence to oral anticoagulants therapy: comparison between vitamin K antagonists and direct oral anticoagulants. Int J Cardiol. 2021;333:162-6.

29. Jackevicius CA, Tsadok MA, Essebag V, Atzema C, Eisenberg MJ, Tu JV, et al. Early non-persistence with dabigatran and rivaroxaban in patients with atrial fibrillation. Heart. 2017;103:1331-8.

30. Lima PR, Gonçalves GM, Rodrigues RC, Oliveira-Kumakura AR. Factors related to patient adherence to the use of new oral anticoagulants. Rev Esc Enferm USP. 2021;56:e20210191.

31. Tarn DM, Shih K, Tseng CH, Thomas A, Schwartz JB. Reasons for nonadherence to the direct oral anticoagulant apixaban: a cross-sectional survey of atrial fibrillation patients. JACC Adv. 2023;2:100175.

32. Suescún-Carrero SH, Niño CM, Ucros-Álvarez A, Robles-Ríos J. Factores relacionados con la adherencia al tratamiento de tuberculosis en el departamento de Boyacá. Rev Méd Risaralda. 2024;30:7-19.

33. Mathew JL, Patel PN, Wagner AL, Suri V, Bharti B, Carlson BF, et al. Analysis of reasons for loss to follow up in a prospective study in Chandigarh, India and impact from telecom changes. BMC Res Notes. 2021;14:419.

34. Mejía-Mejía A, Sánchez-Gandur AF, Tamayo-Ramírez JC. Equidad en el acceso a servicios de salud en Antioquia, Colombia. Rev Salud Pública. 2007;9:26-38.

35. Becattini C, Giustozzi M, Ranalli MG, Bogliari G, Cianella F, Verso M, et al. Variation of renal function over time is associated with major bleeding in patients treated with direct oral anticoagulants for atrial fibrillation. J Thromb Haemost. 2018; 16:833-41.

36. Jackevicius CA, Lu L, Ghaznavi Z, Warner AL. Bleeding risk of direct oral anticoagulants in patients with heart failure and atrial fibrillation. Circ Cardiovasc Qual Outcomes. 2021; 14:e007230.

37. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981-92.

38. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365:883-91.