

Evaluation of secondary prevention of thrombosis in patients from sector III of Zaragoza

Evaluación de la prevención secundaria de trombosis en pacientes del sector III de Zaragoza

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Abstract

Introduction: Venous thromboembolism (VTE) presents a significant clinical challenge, but there is currently a lack of evidence in clinical practice in Spain. **Objective:** To evaluate the epidemiological, clinical, and biological characteristics of patients treated with DOACs for secondary prevention of VTE. **Material and methods:** Descriptive, observational, single-centre, longitudinal and retrospective study of a cohort of 118 patients diagnosed with VTE in sector III of Zaragoza, who were prescribed anticoagulant treatment with direct oral anticoagulants (DOACs) for secondary prevention, from February 2012 to July 2024. **Results:** This study evaluated 118 patients, with 70 receiving rivaroxaban and 48 receiving apixaban. The mean age of the patients was 60.2 years, with significant differences between the treatment groups (rivaroxaban: 59.4 years; apixaban: 65.7 years; $p = 0.0013$). Additionally, 26.3% of patients had risk factors that justified the decision of suggesting anticoagulant treatment. Observed complications included 0.8% of thrombotic events and 9.3% of bleeding events, with no significant differences between groups. This analysis suggests that age and associated risk factors are determinants in the secondary prevention of VTE. **Conclusions:** DOACs administered at secondary prevention doses in selected patients represent an effective and safe alternative for patients at high risk of rethrombosis.

Keywords: Secondary prevention. Venous thromboembolic disease. Deep vein thrombosis. Pulmonary embolism. Direct oral anticoagulants. Risk factor.

Resumen

Introducción: La tromboembolia venosa (TEV) es un desafío clínico significativo con escasa evidencia en la práctica clínica española. **Objetivo:** Evaluar las características epidemiológicas, clínicas y biológicas de pacientes tratados con ACOD para prevenir secundariamente la TEV. **Material y métodos:** Estudio descriptivo, observacional, unicéntrico, longitudinal y retrospectivo en una cohorte de 118 pacientes con TEV del sector III de Zaragoza, tratados con anticoagulantes orales de acción directa (ACOD) para prevención secundaria, entre febrero de 2012 y julio de 2024. **Resultados:** De los 118 pacientes, 70 recibieron rivaroxabán y 48 apixabán. La edad media fue de 60,2 años, con diferencias significativas entre los grupos (rivaroxabán: 59,4 años; apixabán: 65,7 años; $p = 0,0013$). Un 26,3% presentaron factores de riesgo que justificaron el tratamiento anticoagulante. Las complicaciones incluyeron un 0,8% de eventos trombóticos y un 9,3% de eventos hemorrágicos, sin diferencias significativas entre los grupos. La edad y los factores de riesgo son determinantes en la prevención secundaria

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de la TEV. **Conclusiones:** Los ACOD en dosis de prevención secundaria son una alternativa eficaz y segura en pacientes con alto riesgo de retrombosis.

Palabras clave: Prevención secundaria. Enfermedad tromboembólica venosa. Trombosis venosa profunda. Embolia pulmonar. Anticoagulantes orales de acción directa. Factor de riesgo.

Introduction

Venous thromboembolism (VTE) is a condition characterized by the formation of a blood clot in the venous or arterial circulation, disrupting normal blood flow and causing various alterations depending on the type of vessel occluded¹. The main manifestations are deep vein thrombosis (DVT) and pulmonary embolism (PE)².

VTE is the most common acute cardiovascular condition after myocardial infarction and stroke³. In Spain, the incidence rate of DVT ranges between 53 and 162 cases per 100,000 inhabitants, while for PE, it ranges between 39 and 115 cases per 100,000 inhabitants^{4,5}. On the other hand, VTE is also associated with a significant mortality rate, causing more than 370,000 deaths in six European countries⁶. In fact, nearly 20% of patients with PE die within 30 days of diagnosis⁷. Additionally, the incidence of VTE is associated with age, being eight times higher in patients aged 80 compared to those aged 50⁴. Considering that the annual costs associated with hospitalization, preventable expenses, and indirect costs related to the disease are estimated at 8.5 billion euros, it is expected that the burden of these conditions will significantly increase in the coming years for healthcare systems in the predominantly aging populations of the European Union.

DVT typically originates in the valves of the distal deep system of the lower limbs and can progressively extend to the femoropopliteal and ilio-caval regions⁷. Distal forms have less impact, while proximal forms have greater clinical relevance and a higher rate of complications. It can also occur in other areas, such as the upper limbs, the spleno-portal axis, cerebral venous sinuses, or the renal vein². DVT causes partial or complete occlusion of a vein by a thrombus in the extremities and can lead to the detachment of the thrombus or clot, causing PE, infarction, or stroke^{1,2,8}. Its diagnosis is based on pretest probability measured using validated scales (Wells score), D-dimer levels, and Doppler ultrasound^{1,9,10}.

PE is the occlusion of the pulmonary artery lumen by a thrombus formed in situ due to local damage or by a thromboembolism originating from the deep venous system of the lower extremities. The clinical presentation is heterogeneous, with symptoms such as dyspnea,

tachypnea, syncope, and hypotension, and there are even cases of incidental, completely asymptomatic PE. Similar to DVT, the diagnosis is based on clinical suspicion and blood tests to evaluate D-dimer levels, requiring confirmation with imaging, preferably computed tomography angiography, although other methods such as ventilation-perfusion scintigraphy or conventional angiography can also be used¹¹.

VTE is a multifactorial condition that occurs when one or more predisposing factors coincide in an individual: environmental factors and patient-related factors¹. Risk factors can be divided into: 1) identifiable or non-identifiable; 2) transient or permanent; and 3) hereditary or non-hereditary¹². Arterial and venous thrombotic diseases are different expressions of the same disease, so cardiovascular risk factors such as obesity, smoking, dyslipidemia, hypertension, and diabetes mellitus can contribute to the event^{12,13}.

Recurrent VTE is the formation of a thrombus at a later time, regardless of the location of the previous episode, a phenomenon that occurs relatively frequently². The incidence of recurrent VTE does not seem to depend on the clinical manifestations of the first event but often occurs in the same clinical form as the initial event. Additionally, recurrences are closely related to the factor that caused the first episode. In one study, the risk of recurrent VTE after DVT caused by an identifiable and transient risk factor, following the discontinuation of anticoagulation, was 3.3% per patient per year up to 24 months¹⁴. The annual risk of recurrence in cases of VTE with an unidentified risk factor after stopping treatment is 10% within the first years and increases to 50% at 10 years¹⁵. These patients represent 25-30% of all VTE patients¹⁶.

The treatment of VTE is based on early and adequate anticoagulation, divided into three phases: acute (5-21 days), initial (3-6 months), and extended (> 6 months)^{17,18}. Anticoagulant therapy is adjusted according to the type of event, its severity, and patient characteristics. The primary phase lasts 3 to 6 months, which is the minimum recommended duration. After completing the initial treatment, the patient should be reassessed to determine whether indefinite treatment is needed to prevent future thrombotic events, i.e., secondary prevention. However, the initiation of treatment

must always be conditioned by periodic reassessment of thrombotic and hemorrhagic risk¹⁶.

The 2020 American Society of Hematology (ASH) clinical practice guidelines provide recommendations for selecting patients who are eligible for secondary prevention of recurrent thrombosis with extended anti-coagulant therapy¹⁹. The criteria are based on identifying patients with VTE without an identifiable risk factor or with permanent risk factors, and in more difficult or doubtful cases, additional methods such as prognostic scales, D-dimer, or detection of residual venous thrombosis with ultrasound can be used, although these tools should not be used systematically.

Currently, there is no recommendation in clinical practice guidelines on which biological markers are indicators of re-thrombosis, but they can help in decision-making, so their determination is part of the thrombotic risk assessment of patients. D-dimer, a marker of fibrinolysis, can help evaluate the risk of recurrence along with another inflammatory marker such as factor VIII^{20,21}.

Anticoagulant therapy can be administered injectably with heparins or fondaparinux, or orally with vitamin K antagonists (VKAs) or direct oral anticoagulants (DOACs)^{10,22}.

Long-term treatment with VKAs is often associated with significant limitations, such as the need for laboratory monitoring of the International Normalized Ratio (INR), which increases the complexity of therapeutic management²³. In contrast, DOACs represent an improvement in the treatment of these patients due to their rapid onset of action, favorable pharmacokinetics, and predictable oral bioavailability, eliminating the need for monitoring^{10,24}. Additionally, compared to VKAs, DOACs have fewer interactions when administered concomitantly with other drugs²⁵. In fact, current clinical practice guidelines recommend DOACs over VKAs with a level of recommendation and evidence of Ia for all phases of treatment^{19,25-27}.

In Spain, DOACs are only funded for stroke prevention and systemic embolism in patients with non-valvular atrial fibrillation with one or more risk factors²⁸, and for VTE prophylaxis in elective hip or knee replacement surgery²⁹. Consequently, access to these drugs for patients with DVT or PE has been limited due to their higher short-term cost compared to the therapeutic alternative (VKAs)³⁰⁻³².

Therefore, the objective of this study is to evaluate the epidemiological, clinical, and biological characteristics of patients treated with DOACs for secondary prevention of VTE, to gain a better understanding of

their safety and effectiveness in routine clinical practice in Spain.

Method

Study design

We conducted a descriptive, observational, single-center, longitudinal, and retrospective study of a cohort of 118 patients diagnosed with VTE in Sector III of Zaragoza who have an indication for anticoagulant treatment as secondary prevention.

The list of patients, as well as epidemiological, clinical, and biological data, were retrospectively obtained from the electronic medical records of patients seen at the Hospital Clínico Universitario Lozano Blesa in Zaragoza (Spain), in the hemostasis and thrombosis clinic of the hematology department. Data collection period was from February 2012 through July 2024.

Authorization for the research was obtained from the Sector Zaragoza III through the center's administration.

Study population

The study included 118 patients over 18 years of age who had suffered VTE and were undergoing treatment with DOACs for secondary prevention in Sector III of Zaragoza, with a minimum follow-up of 6 months and a 15-day window. Patients who initiated secondary prevention treatment between February 2012 and December 2023 were included. Patients who refused anticoagulant treatment and those with an identifiable VTE risk factor or a causative pathology justifying other treatment or its discontinuation were excluded.

Data collection

Data were collected from the database of the hemostasis and thrombosis clinic of the hematology department at the Hospital Clínico Universitario Lozano Blesa in Zaragoza, Spain corresponding to Sector III of Aragon. To preserve patient privacy, a pseudonymization process was implemented, replacing identifiable information with unique codes so that the data could not be directly linked to specific individuals without additional information. The data were stored in a secure environment, and only authorized personnel had access to the pseudonymization key. Additionally, all regulations established by the General Data Protection Regulation of the European Union were followed to ensure the protection and privacy of personal data.

Table 1. Description of sociodemographic variables according to the type of treatment received in secondary prevention

Variable	Apixaban	Rivaroxaban	Total	p
Age (years) at which thrombosis occurred				
Mean (SD)	65.67 (15.61)	56.39 (15.72)	60.16 (16.27)	0.0013
Valid n	48	70	118	
Age groups (years)				
< 40	3 (6.3%)	48	11 (15.7%)	0.0015
40-49	7 (14.6%)	48	7 (10.0%)	
50-59	5 (10.4%)	48	15 (21.4%)	
60-69	8 (16.7%)	48	25 (35.7%)	
70-79	15 (31.3%)	48	8 (11.4%)	
≥ 80	10 (20.8%)	48	4 (5.7%)	
Valid n	48	70	118	
Sex, n (%)				
Male	26 (54.2%)	48	48 (68.6%)	0.1119
Female	22 (45.8%)	48	22 (31.4%)	

SD: standard deviation.

Data analysis

In the statistical analysis, the mean and standard deviation were used to present quantitative variables, and percentages were used for qualitative variables. The chi-square test was used to compare categorical variables, and the non-parametric Mann-Whitney test was used to compare continuous variables. The statistical analysis was performed using SAS Enterprise Guide, version 7.15 (SAS Institute, Cary, NC, USA). The significance level was set at $p < 0.05$ for all cases.

Results

Sociodemographic characteristics

Between February 2012 and July 2024, 118 patients meeting the inclusion criteria were evaluated, of whom 70 were treated with rivaroxaban and 48 with apixaban, both drugs aimed at secondary prevention of VTE. Table 1 summarizes the sociodemographic characteristics of the study population. The mean age was 60.2 (± 16.3) years, with a significant difference between treatment groups, being lower in patients treated with rivaroxaban (59.4 ± 15.7 years) than in those treated with apixaban (65.67 ± 15.6 years) ($p = 0.0013$). Additionally, when considering age ranges, most patients treated with rivaroxaban were between 60 and 69 years old (35.7%), compared to 16.7% in the apixaban group ($p = 0.0015$). Of the included patients, 62.7% were men, with no statistically significant differences between the groups in terms of sex ($p = 0.1119$).

Risk factors

Figure 1 shows the reasons for choosing the type of treatment for secondary prevention, with the following distributions: 33.1% of patients had recurrent thrombosis, 24.5% had proximal DVT, 19.5% had isolated PE, and 16.1% had DVT + PE concurrently. Portal thrombosis and DVT + unusual thrombosis were less frequent (4.2% and 2.5%, respectively).

Regarding treatment groups, 40% of patients with recurrent thrombosis were treated with rivaroxaban, and 22.9% with apixaban. In the case of PE, apixaban was administered more frequently to 37.5% of patients, while rivaroxaban was administered to 7.1%. For portal thrombosis, all patients received rivaroxaban (7.1%). For unusual DVT and unusual thrombosis, the distribution was similar: 2.9% of patients were treated with rivaroxaban, and 2.1% with apixaban. Similarly, in cases of DVT + PE, 14.3% of patients were treated with rivaroxaban, while 18.8% received apixaban. For proximal DVT, most patients were treated with rivaroxaban, while 18.8% received apixaban.

The statistical analyses performed were significant for the treatment groups. Among the baseline characteristics of the patients, more patients treated with apixaban had PE (37.5%), while only 7.1% of the rivaroxaban group had PE ($p = 0.0008$); the selection of the drug was based on routine clinical practice.

On the other hand, 64.6% of patients did not have any type of thrombophilia, and no significant differences were found in the presence of thrombophilia between the two groups ($p = 0.6895$). Genetic thrombophilia was

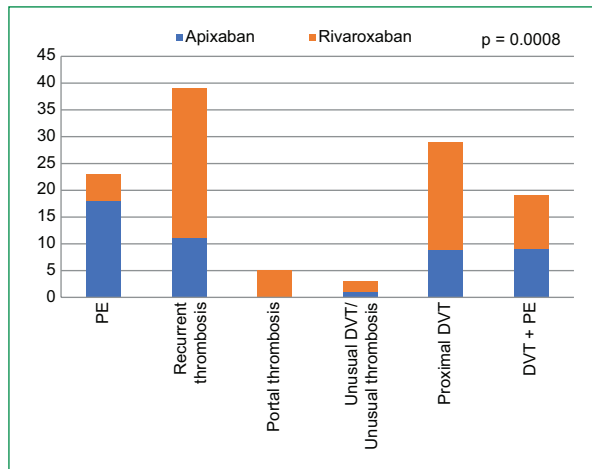


Figure 1. Type of event according to the type of treatment received.

the most common type (55.2%). There were 5 patients with plasma thrombophilia (17.2%), 4 patients with genetic and plasma thrombophilia (13.8%), 3 patients with acquired thrombophilia (10.3%), and 1 patient with genetic and acquired thrombophilia (3.4%).

A total of 26.3% of the sample had a risk factor that favored the decision to maintain anticoagulant treatment beyond 6 months. Among these, systemic disease was the most frequent clinical situation (51.6%). However, a difference was observed between the treatment groups, as 46.7% of patients treated with rivaroxaban had cirrhosis, compared to 0% with apixaban, and 6.7% had reduced mobility, compared to 43.8% with apixaban, resulting in a statistically significant difference ($p = 0.0028$) (Table 2).

The presence of risk factors such as hypertension and dyslipidemia was significantly higher in the apixaban group (60.4% and 58.3%, respectively) than in the rivaroxaban group (37.1% and 35.7%, respectively) ($p = 0.0128$ and $p = 0.0152$) (Fig. 2). Obesity was also more prevalent in the apixaban group (43.8%) than in the rivaroxaban group (12.9%) ($p = 0.0002$) (Fig. 2). Overall, patients treated with apixaban had a higher number of risk factors, with 20.8% of patients having four or more risk factors, compared to 5.7% in the rivaroxaban group ($p = 0.0030$) (Table 2).

Analysis of lab test results and imaging

Table 3 describes the laboratory variables according to the type of secondary prevention treatment. D-dimer levels (ngFEU/mL) measured in the interval between the end of treatment and the decision to initiate secondary

prevention ranged between 29.0 and 2511.0 in the apixaban group and between 79.0 and 3711.0 in the rivaroxaban group. Specifically, the mean D-dimer levels were significantly higher in the apixaban group (691.7 ± 597.2) vs the rivaroxaban group (505.8 ± 609.3) ($p = 0.0338$). The results of the comparison of the remaining variables were not statistically significant.

Most imaging follow-up at 6 months, according to the type of secondary prevention treatment administered, was performed using Doppler ultrasound in 60.2% of patients.

Complications since the initiation of secondary prevention

Patients had a median of 1.8 (1.0-2.6) years of secondary prevention at the time of data extraction. Table 4 presents the different types of complications observed in patients since the initiation of secondary prevention according to the treatment received at that stage. There were 0.8% who experienced a thrombotic event during the observation period and 9.3% who experienced a hemorrhagic event; most of these were minor bleeding (54.5%) (Fig. 3). No statistically significant differences were found between the two groups in terms of the occurrence of these events, nor were there differences in the specific type of hemorrhagic event.

Regarding the mean age of patients without hemorrhagic complications, it was 61.4 (± 15.7) years, while for those with complications, it was 48.2 (± 17.3) years. The difference in mean ages between the two groups was statistically significant ($p = 0.0160$).

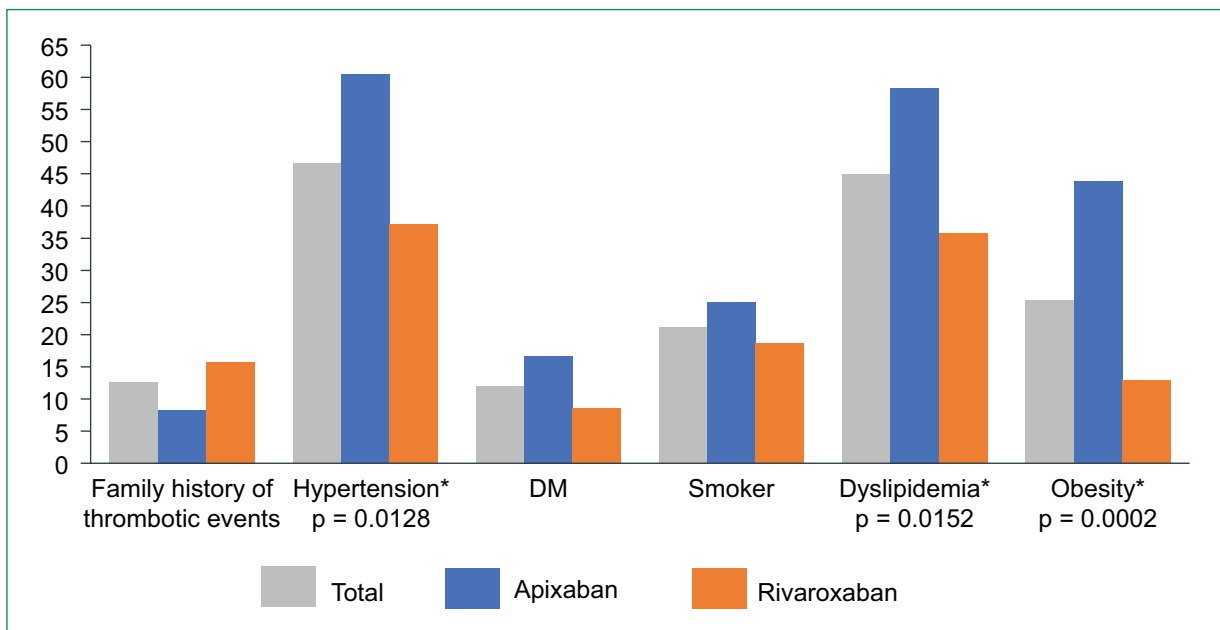
Discussion

Our study provides relevant information on the safety and efficacy profile of these drugs, as well as the clinical and demographic characteristics that may influence their selection and outcomes. The main findings focus on age differences, the incidence of PE, complications, and risk factors associated with treatment with rivaroxaban and apixaban.

The study was conducted in a retrospective cohort of 118 patients undergoing treatment with DOACs for secondary prevention. Of these, 70 received rivaroxaban (10 mg/24 h) and 48 received apixaban (2.5 mg/12 h). The mean age of the patients was 60.2 years, and 62.7% were men (with no significant differences by sex). These data are consistent with the main studies that led to the indication of these drugs, which indicate that the incidence is higher in men across all age

Table 2. Description of clinical variables according to the type of treatment received in secondary prevention

Variable	Apixaban	Rivaroxaban	Total	p
Risk factor favoring the decision to maintain treatment according to clinical situation, n (%)				
No	32 (66.7%)	55 (78.6%)	87 (73.7%)	0.1489
Yes	16 (33.3%)	15 (21.4%)	31 (26.3%)	
Valid n	48	70	118	
Type of risk factor that may have caused or precipitated the thrombotic event, n (%)				
Cirrhosis	0	7 (46.7%)	7 (22.6%)	0.0028
Systemic disease	9 (56.3%)	7 (46.7%)	16 (51.6%)	
Reduced mobility	7 (43.8%)	1 (6.7%)	8 (25.8%)	
Valid n	16	15	31	
Number of risk factors present, n (%)				
0	4 (8.3%)	20 (28.6%)	24 (20.3%)	0.0030
1	6 (12.5%)	13 (18.6%)	19 (16.1%)	
2	14 (29.2%)	24 (34.3%)	38 (32.2%)	
3	14 (29.2%)	9 (12.9%)	23 (19.5%)	
≥ 4	10 (20.8%)	4 (5.7%)	14 (11.9%)	
Valid n	48	70	118	

**Figure 2.** Type of factors that favour the decision to continue treatment.

groups when excluding specific risk factors for women, such as hormonal contraception and pregnancy^{33,34}.

Regarding the presentation of VTE, in our study, 33.1% of patients had recurrent thrombosis, 24.5% had proximal DVT, 19.5% had isolated PE, and 16.1% had concurrent DVT + PE. In our cohort, most patients were under secondary prevention treatment after experiencing more than one episode of VTE, and in the rest, we can conclude that DVT is more frequent

than isolated PE, and the disease often manifests as a combination of DVT + PE. These data are consistent with those provided by studies on the indication of DOACs^{33,34}.

The utility of thrombophilia testing to predict the risk of recurrence remains a debated topic. Receiving a diagnosis and the label of thrombophilia can generate concern and lead to unnecessary interventions for the patient, especially considering that many individuals with low-risk

Table 3. Description of laboratory variables according to the type of treatment received in secondary prevention

Variable	Apixaban	Rivaroxaban	Total	p
D-dimer (ngFEU/ml)				
Mean (SD)	691.65 (597.20)	505.83 (609.31)	582.88 (607.62)	0.0338
Valid n	34	48	82	
D-dimer (ngFEU/mL) - positive/negative, n (%)				
Negative	23 (67.6%)	37 (77.1%)	60 (73.2%)	0.3420
Positive	11 (32.4%)	11 (22.9%)	22 (26.8%)	
Valid n	34	48	82	
Factor VIII, %				
Mean (SD)	198.60 (91.38)	163.29 (31.91)	170.22 (50.18)	0.4336
Valid n	10	41	51	
Factor VIII, % - positive/negative, n (%)				
Negative	7 (70.0%)	40 (97.6%)	47 (92.2%)	0.0037
Positive	3 (30.0%)	1 (2.4%)	4 (7.8%)	
Valid n	10	41	51	
PFA, n (%)				
No	10 (90.9%)	21 (61.8%)	31 (68.9%)	0.1489
Normal	0	8 (23.5%)	8 (17.8%)	
Shortened	1 (9.1%)	5 (14.7%)	6 (13.3%)	
Valid n	11	34	45	

PFA: platelet function analyzer.

Table 4. Description of complications since the start of secondary prevention according to the type of treatment received in secondary prevention

Variable	Apixaban	Rivaroxaban	Total	p
Thrombotic event, n (%)				
No	48 (100.0%)	69 (98.6%)	117 (99.2%)	0.4056
Yes	0	1 (1.4%)	1 (0.8%)	
Valid n	48	70	118	
Hemorrhagic event, n (%)				
No	45 (93.8%)	62 (88.6%)	107 (90.7%)	0.3419
Yes	3 (6.3%)	8 (11.4%)	11 (9.3%)	
Valid n	48	70	118	
Type of hemorrhagic event, n (%)				
Minor hemorrhage	2 (66.7%)	4 (50.0%)	6 (54.5%)	0.7802
Major hemorrhage	0	1 (12.5%)	1 (9.1%)	
Clinically relevant hemorrhage	1 (33.3%)	3 (37.5%)	4 (36.4%)	
Valid n	3	8	11	

thrombophilias, such as heterozygous factor V Leiden, will not develop a VTE event or have an elevated risk of recurrence. Additionally, it is important to note that research on hereditary thrombophilia has primarily focused on Caucasian populations; for example, factor V Leiden is common in this group but extremely rare in non-Caucasian populations³⁵.

Consequently, it is still unclear whether thrombophilia testing influences decisions on the duration of anticoagulation in clinical practice. The goal of genetic thrombophilia testing is to detect currently known hereditary

or acquired prothrombotic states. In our cohort, we identified thrombophilia in 35.4% of patients. However, these findings do not allow decisions on secondary prevention to be based solely on the results of such tests, as only a proportion of patients have thrombophilia. This is consistent with the main studies cited in this discussion, which report approximately 30% of patients with a known prothrombotic state. Such results suggest the likely existence of other unidentified prothrombotic states and support the theory of a multifactorial model in the development of VTE.

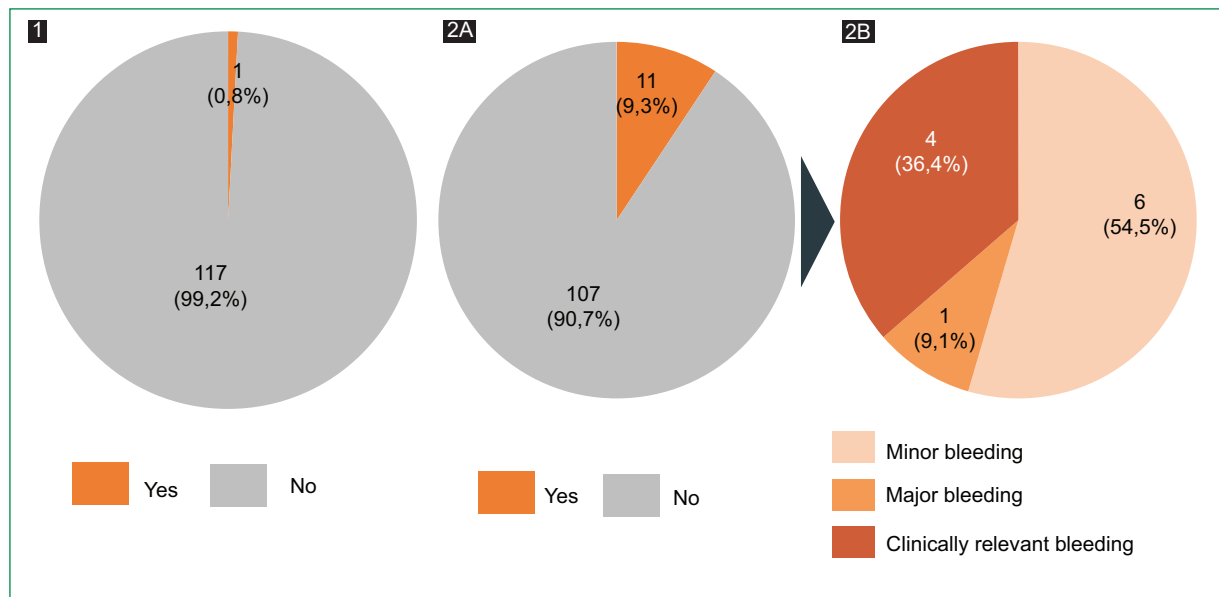


Figure 3. Presence of complications in patients according to type of event. **1:** presence of thrombotic event. **2A:** presence of haemorrhagic event. **2B:** type of haemorrhagic event.

Cardiovascular risk factors are among the causal agents of vascular wall damage that contribute to the occurrence of VTE, making it interesting to study their presence in our series of patients. Most of our patients had hypertension (46.6%) or dyslipidemia (44.9%).

One of the most notable findings was the age difference between the treatment groups, with patients treated with apixaban being significantly older than those in the rivaroxaban group (65.7 vs. 59.4 years; $p = 0.0013$). This could be explained by differences in tolerability or clinical preferences, as apixaban is often recommended in older patients due to its more favorable bleeding risk profile.

The higher number of patients with PE in the apixaban group (37.5% vs. 7.1%; $p = 0.0008$) raises important questions. It is possible that patients treated with apixaban had baseline characteristics of higher risk, such as obesity (43.8% vs. 12.9%; $p = 0.0002$) or hypertension (60.4% vs. 37.1%; $p = 0.0128$), which may predispose them to a higher incidence of PE. These results reinforce the need to individualize anticoagulant treatment, considering the thrombotic and hemorrhagic risk profile of each patient.

Regarding complications, the overall rate of hemorrhagic events was 9.3%, while recurrent thrombotic events were rare (0.8%). Although no significant differences were observed between the groups in this regard, the findings confirm that DOACs are a safe option in clinical practice, aligning with previous studies

that have demonstrated their efficacy and lower need for monitoring compared to VKAs.

Patients had a median of 1.8 (1.0-2.6) years of secondary prevention at the time of data extraction. In registry studies, a duration of 24 months is tested, allowing us to confirm that the extension of anticoagulation for secondary prevention is safe and does not lead to a higher occurrence of thrombotic, hemorrhagic, or other events that would justify its discontinuation or a change in treatment^{33,34}.

Compared to the existing literature, the results obtained align with the 2020 ASH guidelines, which highlight DOACs as the preferred option for secondary prevention of VTE due to their safety and efficacy profile.

This study contributes to clinical knowledge by focusing on the Spanish population, whose access to these drugs has been limited by economic and funding issues. Additionally, data on risk factors such as obesity, dyslipidemia, and reduced mobility support previous research emphasizing the importance of evaluating the patient's clinical context before initiating therapy.

The main limitations of this study are the small sample size, likely due to the funding situation of these treatments in our setting, and the retrospective, single-center design, which may also limit the generalizability of the findings to other populations. Additionally, the lack of information on treatment adherence could have influenced the results. Finally, although significant differences were identified between the groups, it is

important to consider that these could be due to uncontrolled factors in the analysis, such as the initial severity of VTE or differences in clinical management.

Conclusions

DOACs at secondary prevention doses are a safe and effective alternative for patients requiring long-term treatment. The results of our study indicate that the selection of this treatment should be based on a comprehensive evaluation of the patient, considering thrombotic risk factors, demographic characteristics, and individual preferences, and its indication should be constantly reevaluated during patient follow-up.

Multicenter and prospective studies are needed to confirm these findings and address the limitations of the present study.

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Conflicts of interest

C. Navas and M. Lloret-Avellá are employees of IQVIA Information S.A.

Ethical considerations

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality, informed consent, and ethical approval. The authors obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data, so informed consent was not required. Relevant recommendations were followed.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, Tables, or their corresponding captions.

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