Influence of the COVID-19 pandemic on patients receiving oral anticoagulants for the treatment of non-valvular atrial fibrillation

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Introduction

- AF is a disabling condition and causes up to 30% of strokes[1]. The prevalence of AF in Spain is 4.4% in people aged >40 years, and most of them suffer non-valvular AF (NVAF)[2-4].
- Vitamin K antagonists (VKA) and the new direct-acting oral anticoagulants (NOAC) are the most used in NVAF patients[5,6].
- COVID-19 has implied a considerable burden for European countries, particularly in Spain[7,8]. It also had many health, social and economic consequences, including the pressure on healthcare systems[9,10].
- Since the treatment with VKAs require frequent monitoring to avoid thromboembolic and bleeding events, NOACs were recommend in NVAF during the COVID-19 pandemic[11,12].

Objective

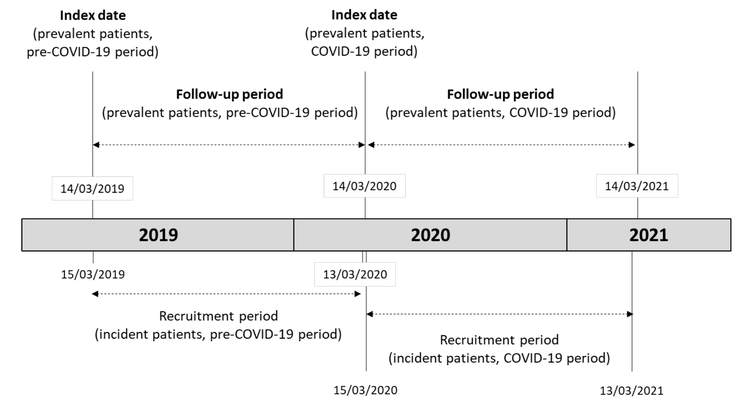
- This study aims to evaluate the impact of the pandemic in patients with NVAF receiving anticoagulant treatment with VKA or NOAC in clinical practice in Spain.

Methods

Design of the study

- This is an observational, retrospective study based on the electronic medical records (EMRs) of the BIG-PAC database[13].
- EMRs undergo rigorous anonymization in the centers of origin, in compliance with Spanish regulations.
- The study considered two periods (pre-COVID-19 and COVID-19) and two cohorts of patients with NVAF (Figure 1).
  - Prevalent patients were those on treatment with oral anticoagulant treatment (NOAC or VKA) and were followed until the discontinuation of the anticoagulant treatment, the end of the study period (12 months), or death, whichever occurred first.
  - Incident patients were those who started a new oral anticoagulant treatment (NOAC or VKA) during the recruitment period.

Figure 1. Study design



Study variables

- Demographic characteristics, comorbidities, effectiveness, treatment patterns and healthcare resources utilization were analyzed. The results in prevalent patients were compared between the pre-COVID-19 and the COVID-19 periods, and the anticoagulation treatment that led to their inclusion in the study. The treatment patterns of incident patients in the study periods were also compared.

Results

Characteristics of prevalent patients

- On average, prevalent patients were 77.2 years old and 54.2% of patients were male. The median time from diagnosis was higher during the COVID-19 period), in comparison to the pre-COVID-19 period (1,704.5 days vs. 1,582.0 days; p<0.001).
- In general, the study population analyzed during the pandemic had more comorbidities; arterial hypertension, dyslipidemia, and diabetes were identified as the most frequent disorders. Charlson comorbidity index and CHAS2DS2-VASc and HAS-BLED scores were also higher in NVAF patients during the COVID-19, compared to those in the previous period (p≤0.001 in all comparisons) (Table 1).

Table 1. Characteristics of prevalent patients

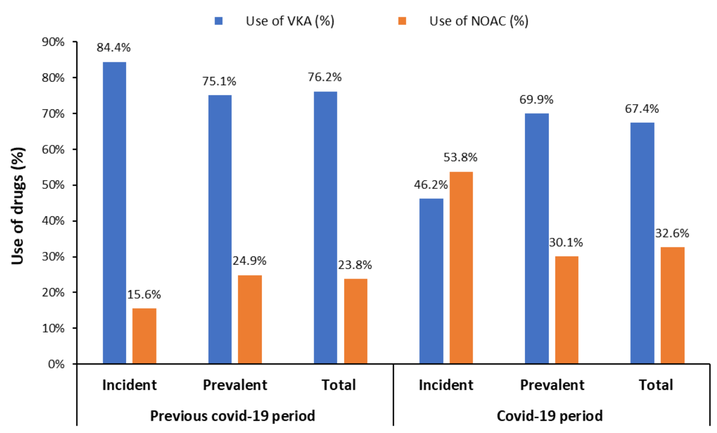
Study groups	Pre-COVID-19 period	COVID-19 period	Total	p
Number of patients, n (%)	12336 (48.0)	13342 (52.0)	25678 (100.0)	
Age, years, mean (SD)	77.1 (9.8)	77.3 (9.8)	77.2 (9.8)	0.082
Gender male, n (%)	6710 (54.4)	7217 (54.1)	13927 (54.2)	0.628
Time from diagnosis, days				
Mean (SD)	1510.4 (857.2)	1664.7 (976.9)	1590.6 (924.6)	<0.001
Median (P25-P75)	1582.0 (730.0 - 2354.0)	1704.5 (766.0 - 2641.0)	1634.0 (750.0 - 2472.0)	
Clinical variables				
BMI, kg/m^2, mean (SD)	30.1 (5.1)	29.2 (5.3)	29.6 (5.2)	<0.001
Hemoglobin, g/dL, mean (SD)	14.2 (1.8)	14.1 (1.8)	14.2 (1.8)	<0.001
Scales				
CCI, mean (SD)	1.9 (1.7)	2.0 (1.7)	2.0 (1.7)	<0.001
CHAS$_2$DS$_2$-VASc, mean (SD)	2.8 (1.4)	2.9 (1.4)	2.8 (1.4)	0.001
HAS-BLED, mean (SD)	3.0 (0.9)	3.1 (0.9)	3.1 (0.9)	<0.001

BMI: body mass index; CCI: Charlson comorbidity index; P: percentile; SD: standard deviation.

Use of medications in incident and prevalent patients

- The consumption of NOAC rose during the pandemic, with a higher increase in incident patients vs. prevalent patients (Figure 3).
- Apixaban was the most prescribed NOAC, followed by other alternatives such as dabigatran, rivaroxaban and edoxaban.
- Patients with NOAC were more persistent at 12 months than those receiving VKA (pre-COVID-19 period: 78.9% vs. 52.1%, p<0.001; COVID-19 period: 80.3% vs. 49.2%, p<0.001). The duration of treatment was close to the length of the follow-up period in prevalent patients.
- Patients with NVAF were on treatment with an average of at least 3 concomitant medications, mainly renin-angiotensin system acting agents, beta-blockers and nonsteroidal anti-inflammatory drugs.

Figure 3. Use of anticoagulant treatments and treatment durations



Discontinuations were more frequent in incident patients, and in those treated with VKA vs. NOAC (Table 2).

Table 2. Characteristics of prevalent patients

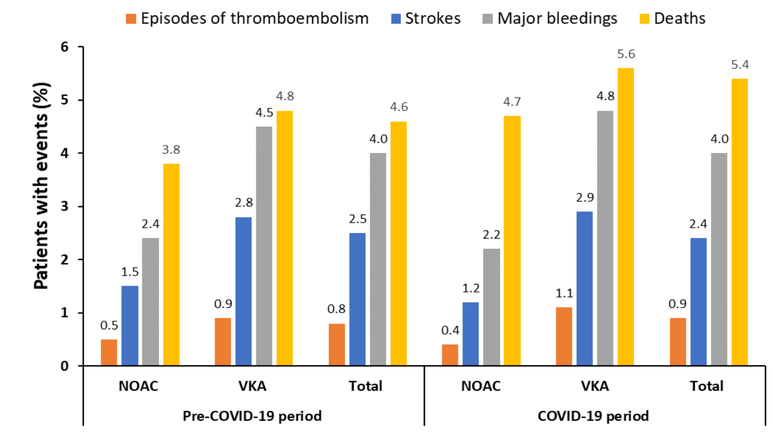
Study populations		Previous covid-19 period			Covid-19 period		
		Incident	Prevalent	Total	Incident	Prevalent	Total
Number of patients, n (%)		1612 (11.5)	12336 (88.5)	13948 (100)	1602 (10.7)	13342 (89.3)	14944 (100)
VKA	**Discontinuation, n (%)**	445 (32.7)	1473 (15.9)	1918 (18.0)	296 (40.0)	1654 (17.7)	1950 (19.4)
	New event*	177 (21.6)	805 (18.1)	982 (18.6)	139 (22.8)	880 (18.6)	1019 (19.0)
	Switch to antiplatelet/anticoagulant	196 (23.9)	339 (7.6)	535 (10.2)	134 (22)	396 (8.4)	530 (9.9)
	Treatment abandonment	375 (45.7)	2973 (66.9)	3348 (63.6)	314 (51.5)	3087 (65.1)	3401 (63.6)
	Death	72 (8.8)	329 (7.4)	401 (7.6)	23 (3.8)	378 (8)	401 (7.5)
NOAC	**Discontinuation, n (%)**	83 (33.1)	329 (10.7)	412 (12.4)	213 (24.7)	394 (9.8)	607 (12.5)
	New event*	38 (22.2)	151 (23,3)	189 (23,1)	120 (16,3)	189 (23,9)	309 (20,2)
	Switch to antiplatelet/anticoagulant	36 (21.1)	78 (12,1)	114 (13,9)	48 (6,5)	49 (6,2)	97 (6,3)
	Treatment abandonment	88 (51.5)	318 (49,1)	406 (49,6)	525 (71,1)	396 (50,1)	921 (60,3)
	Death	9 (5.3)	100 (15,5)	109 (13,3)	45 (6,1)	156 (19,7)	201 (13,2)

*New events such as hemorragic/ischemic strokes or bleedings. NOAC: new direct-acting oral anticoagulants; VKA: vitamin K antagonists.

Cardiovascular events and deaths

- The incidence rate of severe events was slightly higher in the COVID-19 period vs. the pre-COVID-19 period (7.7% vs. 7.0%, respectively).
- Patients on treatment with VKA had more strokes and major bleedings vs. those receiving NOAC (p<0.001 in all comparisons). In addition, VKA patients had more episodes of thromboembolism than NOAC patients during the pandemic (p<0.001) (Figure 2).

Figure 2. Incidence of cardiovascular events and deaths

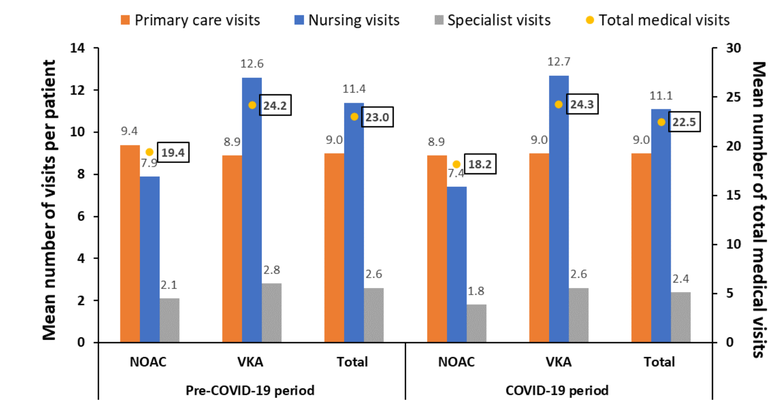


All comparisons NOAC vs. VKA are significant (p<0.05), except for episodes of thromboembolism in the pre-COVID19 period (p=0.051).

Use of healthcare resources in prevalent patients

- The attendance to medical visits (primary care, nursing, and specialist visits) decreased during the pandemic (Figure 4).
- Patients with VKA required more medical visits per year than those on treatment with NOAC (Figure 4).
- During the pre-COVID-19 period, there were no differences in hospital admissions (p=0.404), but VKA patients required more hospitalizations compared to NOAC patients during the pandemic (8.7% vs. 5.7%); p<0.001).

Figure 4. Medical visits in prevalent patients



All comparisons NOAC vs. VKA are significant (p<0.05), except for primary care visits in the COVID-19 period (p=0.498).

Conclusions

During the COVID-19 pandemic, the consumption of NOAC increased in patients with NVAF, who had a higher persistence to the treatment (>70%). There was also an increase in the cardiovascular events and deaths, whereas the attendance to medical visits decreased during the pandemic.

References

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Disclosures

This study was sponsored by BMS-Pfizer Alliance. Dr. J. Comín-Colet reports fees as a coordinator investigator of this study by Pfizer and Bristol Myers Squibb. Antoni Sicras is an Atrys Health employee, CRO of the study. Inés Pérez Román is an Atrys Health employee, CRO of the study. Joel Salazar-Mendiguchía reports that he is a Bristol Myers Squibb employee and has BMS stocks. Isabel del Campo Alonso reports that she is a Bristol Myers Squibb employee has BMS stocks. Ainara Echeto reports that she is a Bristol Myers Squibb employee has BMS stocks. David Vilanova Larena reports that he is a Bristol Myers Squibb employee has BMS stocks. Dra. Olga Delgado Sánchez reports fees as a coordinator investigator of this study by Pfizer and Bristol Myers Squibb.

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