Real-life Safety and Effectiveness of Apixaban in Patients with Non-Valvular Atrial Fibrillation

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INTRODUCTION

Real-world data on long-term safety and effectiveness in clinical practice of novel oral anticoagulants (NOACs) play an important role in the assessment of risks and benefits of this class of drugs and in supporting decision making process. Despite this, currently, the real world evidence on NOACs is still limited and available data refer mostly to administrative or insurance databases. This study aimed to collect data from Italian hospitals on patients with non-valvular atrial fibrillation (NVAF) to evaluate the incidence of major bleeding and cardiovascular outcomes in a cohort of patients exposed to apixaban.

OBJECTIVE

Our primary objective was to evaluate the incidence of major bleedings during treatment with apixaban in patients with NVAF. As a secondary objective, we investigated the incidence of a composite endpoint of major events including all-cause death, myocardial infarction, stroke and systemic thromboembolism.

METHODS

In this multi-centre, retrospective, observational study we collected data from clinical database on consecutive patients with a diagnosis of NVAF, aged 18 years or older who were newly prescribed with in the period from 1st of January 2014 till 31st of March 2016. The follow-up began at the first visit of the patients and underwent up to 3 follow-up visits. Each patient had to attend at least one follow-up visit during the observation period, the maximum length of follow-up was 3 years. Patients were excluded if they had been treated with apixaban in the 12 months before the beginning of the study or if they were diagnosed with valvular AF (with a prosthetic heart valve or with mild/severe mitral stenosis). The study protocol and CRF developed specifically for this study were approved by the Ethics Committee of each study centre. Several characteristics of the patients were collected including apixaban dosage, previous co-morbidities and co-treatments and the occurrence of several outcomes including cardiovascular outcome, death and bleeding were registered.

Descriptive statistics of patients' characteristics were carried-out; in particular frequency and percentage were reported for the categorical variable.

The outcome incidence was calculated both as incidence rate (ratio between number of events occurred during follow-up and person-years accounted by the entire cohort) and as cumulative incidence using the Kaplan-Meier method.

RESULTS

The sample comprised of 766 patients with NVAF from five Italian hospitals. The mean age of patients was 74.2 years and 53.5% were women. The median $CHADS_2$ and CHA_2DS_2VASc scores were respectively 2.0 and 4.0. The most frequent co-morbidities were cardiovascular diseases (hypertension – affecting 84.1% of patients; previous vascular disease [34.1%]; heart failure [22.1%]), renal impairment (30.4%), diabetes mellitus (22.5%) and anaemia (12.5%).

At baseline, 15.7% of patients had a history of at least one major event including stroke, transient ischemic attack or systemic embolism.

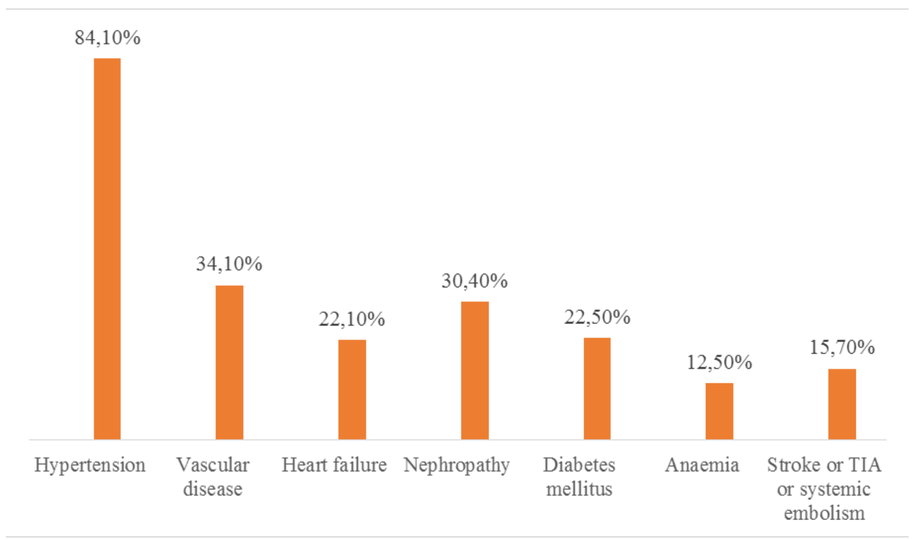

Figure 1. Co-morbidities affecting patients at baseline.

In the whole cohort, half of patients (50.7%) were naïve to oral anticoagulants, while 219 patients had been previously treated with warfarin, heparin (66 patients), acetylsalicylic acid (52 patients), clopidogrel (1 patient) and a novel oral anticoagulant (NOAC, 40 patients). At treatment initiation, 76.5% of patients received the recommended daily dose of 10 mg, while the remaining patients (23.5%) were treated with 5 mg daily.

16 major bleeding events occurred during the follow up period. The incidence rate for major bleeding or bleeding requiring hospitalisation (per 100 patient-years) was 1.19, while the overall major bleeding cumulative incidence was 8.5% (95%CI 3.8%-18.6%) with a 3-year observational period as shown in Figure 2. The major bleeding rate for those patients who completed all the 3-year observation period was 4.4% (95%CI 1.6%-12.0%).

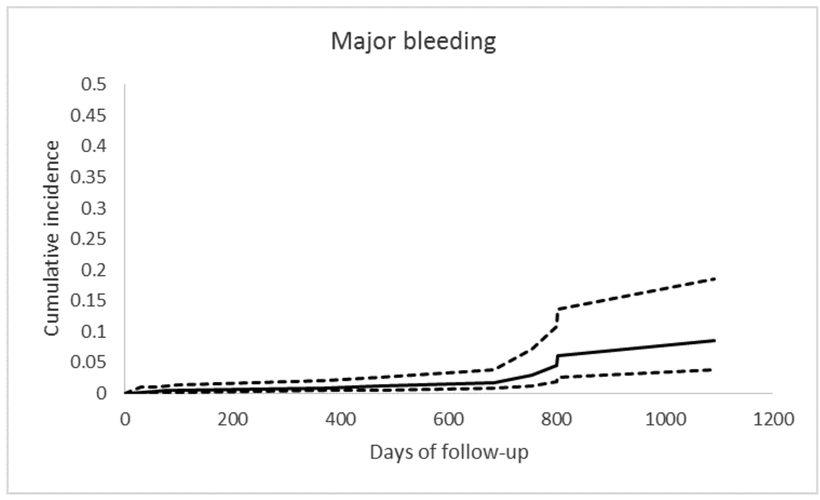

Figure 2. Cumulative incidence of major bleeding by the end of the observation period (Kaplan-Meier).

A major bleeding event was reported during the first follow-up visit (V1) by 13 patients out of 750 (1.7%), by none of the 253 patients attending the second follow-up visit (V2), and by 3 of the 84 patients (3.6%) who attended the third follow-up visit (V3) (Table 1).

Location of 13 major bleeds reported at V1 was eye (2 cases), retroperitoneal space (2), muscles (1), and gastrointestinal tract (1), while no data were provided for the remaining cases. Of the 3 major bleeds reported at V3, 1 patient had both gastrointestinal and subcutaneous bleeding, while 2 were intracranial and eye bleeding.

Regarding the composite endpoint, 32 events were reported at the end of the follow-up period: 22 deaths, 5 MIs, 4 ischaemic strokes, and 1 systemic embolism (Table 1).

The major event rate was 2.6 per 100 patient-years, while the cumulative incidence considering the entire 3-year follow-up period was 6.7% (95%CI 4.4-10.1).

Follow-up visits	V1	V2	V3
Patients	750	253	84
Major Bleeding	13 (1.70)	0 (0.00)	3 (3.57)
Major events (%)			
Death	16 (2.1)	5 (2.0)	1 (1.19)
MI	3 (0.4)	1 (0.4)	1 (1.19)
Ischaemic stroke	3 (0.4)	1 (0.4)	0 (0.00)
Haemorrhagic stroke	0 (0.0)	0 (0.0)	0 (0.00)
Systemic embolism	0 (0.0)	1 (0.4)	0 (0.00)

Table 1 – Number of major bleeding and major events.

CONCLUSIONS

In the present study, the rate of major bleedings and major thrombotic events in real-life patients treated with apixaban was comparable to that found in randomized clinical trial (1).

REFERENCES

1. Granger CB, Alexander HJ, McMurray JJV, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med, 2011;365:981-92.