**A Nurse-led Atrial Fibrillation Clinic: Impact on Anticoagulation Therapy and Clinical Outcomes**

**Running title:** A Nurse-led Atrial Fibrillation Clinic

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**Abstract**

**Background:** Nurses play a central role in the management of atrial fibrillation (AF) patients. An unresolved question is whether a nurse-led clinic would improve clinical outcomes. Herein, we investigated the impact of a nurse-led clinic on anticoagulation therapy and clinical outcomes in a cohort of naïve AF patients.

**Methods:** Prospective study including AF patients starting vitamin K antagonists (VKAs) into a nurse-led AF clinic. These patients were followed in this specific AF clinic. Additionally, AF patients already taking VKAs for 6 months followed according to the routine clinical practice were included as comparison group. The quality of anticoagulation was assessed at 6 months. Efficacy and safety endpoints were recorded during follow-up.

**Results:** We included 223 patients (Nurse-led clinic: 107; Usual care: 116). The mean time in therapeutic range and the proportion of INRs within the therapeutic range were similar in both groups. During 2.06 (IQR 1.01-2.94) years of follow-up, 64 (28.7%) patients changed to direct-acting oral anticoagulants. The proportion of switchers was higher in the nurse-led clinic (37.4%) than in the usual care group (20.7%) (p=0.006) and these patients spent less time to switch (2.0 [IQR 0.7-2.9] *vs*. 6.0 [IQR 3.7-11.2] years; p<0.001). Importantly, the annual rate of ischemic stroke/TIA was significantly lower in the nurse-led clinic (0.47%/year *vs*. 3.88%/year, p=0.016), without differences in the safety endpoints.

**Conclusion:** A nurse-led AF clinic may offer a more ‘patient-centered’ review and holistic follow-up, and it would be associated with a reduction of ischemic stroke/TIA, without increasing bleeding complications. Further studies should confirm these results.

**Keywords:** atrial fibrillation, nurses, outcomes, anticoagulation, hemorrhage, stroke.

**What’s already known about this topic?**

* Nurses play a key role in all areas of the management of AF and are central to the holistic approach of AF.
* The ESC guidelines for the management of AF suggest that specially trained nurses could carry out a regular follow-up of patients.
* An unresolved question is whether a nurse-led clinic would result in better clinical outcomes.

**What does this article add?**

* A nurse-led AF clinic includes a patient-centered approach, a holistic management and more carefully reviews and follow-ups of patients with AF.
* This study shows that a nurse-led AF clinic would be associated with lower ischemic stroke/TIA rates.

**Introduction**

Atrial fibrillation (AF) is the most frequent arrhythmia worldwide and it is associated with increased risk of stroke, thromboembolism and mortality.1 Nevertheless, these risks can be reduced by using oral anticoagulation (OAC), both Direct Oral Anticoagulants (DOACs) or Vitamin K Antagonists(VKAs).2 Despite the increasing use of DOACs, VKAs (mainly warfarin and acenocoumarol) are still widely used for stroke prevention in AF in several countries. Notwithstanding, the efficacy and safety of VKAs depend upon the quality of anticoagulation control, as reflected by the average time in therapeutic range (TTR) of international normalized ratio (INR) 2.0-3.0.

Most AF patients are elderly and have multiple comorbidities. For this reason, the management of AF is complex and should be holistic, including lifestyle modifications. Indeed, during the last years, new approaches to AF management, including the use of novel technologies and a more structured integrated to AF care, are proposed to optimize treatment options for AF.3 Such integrated care aims to address risk factors in a holistic manner —management of blood pressure, heart failure, diabetes mellitus, sleep apnoea, and underlying cardiac ischaemia— with the goal of reducing stroke and cardiovascular burden.4-6 Nurses may play a key role in all areas of the management of AF patients and they are central to the holistic approach of AF management. They are usually the healthcare professionals producing most confidence to patients and this is often translated into better guideline adherence, which leads to significantly improved clinical outcomes.7-9 Indeed, the 2016 European Society of Cardiology (ESC) guidelines for the management of AF already suggests that regular follow-up could be undertaken by specially trained nurses.10 However, an unresolved question is whether a nurse-led clinic with a more carefully review and follow-up of AF patients, would result into better clinical outcomes.

In the present study, we aimed to identify factors associated with poor quality of anticoagulation with VKAs (assessed by the TTR and the Proportion of INRs within the therapeutic Range [PINRR]), and to investigate if a nurse-led AF clinic was associated with a positive impact on the quality of anticoagulation therapy, the prescription of DOACs and clinical outcomes in a consecutive cohort of naïve AF patients starting VKAs in comparison with patients followed-up acording to the routine clinical practice.

**Methods**

This is a prospective observational study including consecutive patients with non-valvular AF from January 27, 2015 to May 30, 2017, performed in a tertiary hospital in the South-eastern of Spain.

To be involved in the study, all patients had to be ≥18 years old, primary diagnosis of AF documented on a 12-lead electrocardiogram (ECG), and sign the informed consent, with no other pre-specified inclusion criteria. Patients with prosthetic heart valves or rheumatic AF, life expectancy lower than 12 months, participating in a clinical trial or other interventional studies, living in a nursing home or under DOAC therapy at inclusion, were excluded.

*Clinical follow-up*

Once potential patients were identified, they were referred to the nurse-led AF clinic and provided signed informed consent. Patients included in this nurse-led AF clinic where naïve AF patients who started treatment with a VKA for the first time, all derived from the Emergency Department of our hospital.

The nurse-led AF clinic was an “outpatient” clinic, specifically designed for this study. Nurses with specific training and experience in the management of AF patients were responsible for this clinic, and it was entirely managed by them. However, they had the support of cardiologists who revised the medical therapy and collaborated in decision-making. .11

The follow-up was performed by in-person visits to the nurse-led AF clinic every 6 months. During these visits, patients were interviewed about AF symptoms and complications. They were also re-educated about AF, anticoagulation, and other associated comorbidities. Indeed, a review of the overall treatment, comorbidities and lifestyle was carried out at every visit. In addition, all medical records were also reviewed to check for possible missing information. With these data, the responsible nurses wrote a clinical report with the possible incidents that occurred, the quality of the anticoagulation and the clinical events suffered by the patients since the last visit. These reports were subsequently reviewed by the cardiologists collaborating in the study. Visits were scheduled to last at least 30 minutes and patients were informed that they could contact the nurse in-person or by telephone between planned visits if needed. Patients attended up to 4 visits in the nurse-led clinic.

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Additionally, we included a group of patients with AF who were under treatment with VKAs during at least the previous 6 months. Therefore, these were not anticoagulation naïve AF patients and were already followed-up in the outpatient cardiology clinic or the anticoagulation clinic. This was only to allow comparisons between baseline clinical characteristics, quality of anticoagulation and clinical outcomes suffered, but as this was not a randomized trial, no randomization was performed. These patients had to sign the inform consent, but were followed according to the routine clinical practice through routine visits to the outpatient cardiology clinic or the primary care physician, and not in the nurse-led AF clinic. Visits were scheduled every 15 minutes. In this group of patients, the information was collected from the hospital electronic medical records or, when unavailable, by telephone interview. No specific follow-up visits were performed regarding the study.

At inclusion, a complete medical history including clinical and demographic data was recorded for all patients. Stroke risk was assessed by the CHA2DS2-VASc score, whereas the bleeding risk was assessed according to the HAS-BLED score. The ‘Labile INR’ criterion for patients from the nurse-led clinic (i.e. naïve patients) was quantified as 0, as no patient was previously anticoagulated. The SAMe-TT2R2 (one point for female Sex; Age <60 years; Medical history [more than two of the following comorbidities: hypertension, diabetes, coronary artery disease, peripheral artery disease, heart failure, stroke, pulmonary, hepatic, or renal disease]; Treatment [interacting medications e.g. amiodarone]; and two points for Tobacco use and non-Caucasian Race) was also calculated to predict poor INR control with VKAs.12

In both, the nurse-led AF clinic and usual care groups, the choice of the appropriate therapy and medication prescriptions were at the discretion of the physician responsible for the patient. Patients in either group were followed-up for two years and the last follow-up was performed on November 18, 2018.

*Quality of anticoagulation*

In both groups of patients, INR controls were performed in the anticoagulation clinic depending on the INR result, as per usual care. The therapeutic range for AF patients taking VKAs is an INR between 2.0 and 3.0. The TTR was used as a way to assess the quality of anticoagulation control, and was calculated by the method of Rosendaal 13 and by the Proportion of INRs within the therapeutic Range (PINRR), also known as direct method. The TTR by the method of Rosendaal was calculated by adding INR measurement frequency and their values, and assuming that changes between consecutive INR measurements are linear over time. The PINRR evaluates the percentage of INR measurements between 2.0 and 3.0 over the total number of INR measurements. Poor anticoagulation quality was defined as a TTR <65% by the method of Rosendaal or PINRR <60%. The TTR and PINRR were assessed at 6 months of inclusion, avoiding the first month of anticoagulation since this period is largely influenced by the fluctuations dues to treatment initiation rather due to the anticoagulant itself.

*Endpoints*

Endpoints were defined as *efficacy endpoints* or *safety endpoints.* Efficacy endpoints included ischemic stroke/transient ischemic attack (TIA), acute myocardial infarction and mortality. Safety endpoints included bleeding events, categorized as major bleeding and clinically relevant non-major bleeding (CRNMB). Major bleeding was assessed by the 2005 International Society on Thrombosis and Haemostasis (ISTH) criteria, as follows: fatal or symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or intramuscular with compartment syndrome, or bleeding causing a fall in hemoglobin level of ≥20 g/L (1.24 mmol/L) or leading to transfusion of ≥2 units of whole blood or red cells.14 CRNMB was also defined according to the ISTH criteria as any sign or symptom of hemorrhage that does not fit the criteria for the ISTH definition of majorbleeding but does meet at least one of the following criteria: a) requiring medical intervention by a healthcare professional; b) leading to hospitalization or increased level of care; or c) prompting a face to face (i.e., not just a telephone or electronic communication) evaluation.15 The investigators identified, confirmed, and recorded all adverse events, as well as other clinical outcomes.

*Ethical considerations*

The study protocol was approved by the Ethics Committee from Hospital Clínico Universitario Virgen de la Arrixaca and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The protocol was also approved by the Spanish Agency for Medicine and Health Products with resolution of Post‐Authorization Study-Observational type with prospective follow-up (reference FMO-VIK-2014-01). All patients gave informed consent to participation.

*Statistical analysis*

Categorical variables are summarized as frequencies and percentages. Continuous variables were presented as mean ± standard deviation (SD) or median and interquartile range (IQR), as appropriate after tested for normality by the Kolmogorov-Smirnov test.

The Pearson Chi-squared test was used to compare proportions. A multivariate logistic regression model was performed to investigate factors associated with poor quality of anticoagulation, incorporating in the multivariate model only those variables that showed a p-value <0.15 in the univariate analysis. Before this multivariate analysis, multicollinearity between potential predictor variables was assessed based in the variance inflation factor values.

Differences in the TTR or PINRR among patients from intervention and usual care groups were assessed using the Student's t-test. Correlation between the TTR and PINRR was tested using the Pearson's correlation coefficient.

Receiver operating characteristic (ROC) curve was applied to evaluate the predictive ability (expressed as c-indexes) of the SAMe-TT2R2 score for switching the anticoagulation therapy.

Annual event rates with 95% Confidence Interval (CI) were calculated for each cohort as the number of first adverse clinical outcomes divided by the total size of the cohort and then divided by time at risk for adverse clinical outcome within the study period, multiplied by 100. The difference between two annual event rates and the associated p-value was calculated. Differences in event-free survival between both groups of patients were reflected by Kaplan-Meier curves.

A p-value <0.05 was accepted as statistically significant. Statistical analysis was performed using SPSS 22.0 (SPSS, Inc., Chicago, IL, USA) and MedCalc v. 16.4.3 (MedCalc Software bvba, Ostend, Belgium) for Windows.

**Results**

We included 223 patients, 107 (48%) in the nurse-led clinic and 116 (52%) in the usual care group. Both groups were balanced in terms of age (age ≥60 years: 88.7% *vs*.94.8%, p=0.094), sex (males: 54.7% *vs*. 54.3%, p=0.952), most comorbidities and high stroke risk (CHA2DS2-VASc ≥2: 91.6% *vs*. 94.8%, p=0.355). There was a higher proportion of ‘high-risk’ bleeding patients in the usual care group, but this was expected given that these were patients already on VKAs and some of them had previous labile INR (HAS-BLED ≥3: 50.5% *vs*. 75.0%, p<0.001) (Table 1).

Regarding the quality of anticoagulation, the mean TTR in the overall cohort was 54.3±22.4% at 6 months of inclusion, and there were not significant differences in terms of TTR between both groups (54.9±22.8% *vs*. 53.7±22.2%, p=0.700). Similarly, the mean PINRR in the overall cohort was 57.3±24.7%, whereas in the nurse-led clinic was 58.6±24.9% and 56.1±24.6% in the usual care group, with no significant differences (p=0.471). The TTR and PINRR presented a direct correlation (*r* = 0.816, p<0.001).

Of the proportion of patients with suboptimal anticoagulation control, 64.7% of patients from the nurse-led clinic had a TTR <65%, whereas 73.0% of patients from the usual care had a TTR <65% (p=0.192). On the other hand, 43.6% of patients from the nurse-led clinic had a PINRR <60%, while 53.2% of patients from the usual care had a PINRR <60% (p=0.163).

The continuous and categorical TTR and PINRR values were slightly higher in the nurse-led AF clinic, but not significantly different compared to the usual care.

*Factors affecting the quality of oral anticoagulation*

We investigated those factors associated with poor quality of anticoagulation (defined as TTR <65%) in the overall cohort. Thus, we performed a multivariate logistic regression analysis, including variables that showed a p-value <0.15 in the univariate analysis but only three variables reached that p-value; obstructive sleep apnea/chronic obstructive pulmonary disease, CHA2DS2-VASc and HAS-BLED scores. No multicollinearity was found between these predictor variables.

In the multivariate analysis, the HAS-BLED score was independently associated with higher risk of poor quality of anticoagulation, with an odds ratio of 1.45 (95% CI 1.05-2.02, p=0.026) (Table 2).

*Switch of anticoagulant therapy*

Furthermore, we investigated switches of anticoagulant therapy and the relationship with the SAMe-TT2R2 score.

The SAMe-TT2R2 score was associated with higher probability of switching from VKAs to DOACs (HR 1.39, 95% CI 1.09-1.75, p=0.007). The predictive ability of this score for switching was poor and non-significant (c-index 0.554, 95% CI 0.471-0.637, p=0.206). When we analyzed the score as categories, 144 (64.6%) patients had a SAMe-TT2R2 ≥2; of these 42 (29.2%) switched to DOACs, which in proportion was not significantly higher compared to the switchers with SAMe-TT2R2<2 (22, 27.8%) (p=0.835).

Overall, there were 64 (28.7%) patients who changed to DOACs. The proportion of switchers was higher in the nurse-led clinic (40, 37.4%) in comparison to the usual care group (24, 20.7%) (p=0.006). Patients from the nurse-led clinic spent less time to switch since the start of OAC (2.0 [IQR 0.7-2.9] years) than patients from the usual care (6.0 [IQR 3.7-11.2] years) (p<0.001).

*Analysis of adverse events*

A summary of adverse events suffered in both groups of patients during a median follow-up of 2.06 (IQR 1.01-2.94) years is shown in Table 3. Of the effectiveness endpoints, all showed lower annual event rates in patients from the nurse-led clinic as compared to the usual care. The annual rate of ischemic stroke/TIA was significantly lower in the nurse-led clinic (0.47%/year *vs*. 3.88%/year, p=0.016), and the survival analysis also demonstrated higher survival probability in this group (log-rank test p-value=0.030) (Figure 1).

For the safety endpoints, annual event rates of major bleeding, CRNMB, and any bleeding were higher in patients from the nurse-led AF clinic but were not statistically significant.

**Discussion**

In the present study, a significantly higher proportion of patients followed-up in the nurse-led clinic were identified as potential users of DOACs and were derived to switch from VKAs to this antithrombotic regimen. Moreover, the group of patients followed-up in the nurse-led clinic suffered significantly lower ischemic stroke/TIA rates, without an increase in bleeding complications. These results highlight the important role of nurses in all areas of the management of AF patients, including the screening, risk stratification, education and control of anticoagulation therapy.16,17

Despite the introduction of DOACs, the VKAs remain widely used worldwide. However, the therapeutic anticoagulant effect of VKAs is influenced by several factors, thus requiring routine monitoring, as a way to assess the quality of anticoagulation, usually reflected by the TTR. Since the efficacy and safety of VKA is intimately related to TTR, good quality of anticoagulation is the cornerstone of VKA treatment.18,19 Thus, quality of anticoagulation is part of appropriate clinical decision-making and management, and all efforts should be directed to achieve and maintain the highest TTR possible.10,20,21 In this study, the quality of anticoagulation was in accordance with other reports from Spanish populations,22,23 and was similar assessed by the TTR or PINRR, presenting a direct correlation as has been previously observed.22 In addition, it was similar between the nurse-led clinic and the usual care group. On the other hand, we found that the HAS-BLED score was associated with poor quality of anticoagulation. This is not surprising, since higher scores in HAS-BLED imply more comorbidities, which may hamper the achievement of an optimal TTR.22

Regarding the SAMe-TT2R2 score, in this study, we found that higher scores were related to switching, consistent with its original objective that was to predict which patients do well with VKAs, and several studies have demonstrated that it was able to predict poor INR (i.e. poor TTR), thus aiding decision-making.22,24-26 However, the predictive ability of the SAMe-TT2R2 score for switching in the present study was limited, which has also been observed in the past.22,27 Nevertheless, we found higher switching to DOACs in the nurse-led clinic. This is of importance since DOACs have shown a clear benefit over warfarin in terms of safety and efficacy.28-30 It could be hypothesized that the careful and more frequent follow-up provided in the nurse-led clinic may identify potential users of DOACs more easily, for example, because of poor anticoagulation control with VKAs. Given that labile INR or poor anticoagulation quality is associated with a raised risk of adverse events,31,32 such patients would benefit from switching to DOACs. When DOACs are not an available option, the nurse-led clinic could be helpful in reminding patients of the importance of good adherence to VKAs, as well as review of interacting drugs/foods, and those factors affecting the quality of VKA therapy

Nurse-led clinics are of interest in recent years. Previously, some studies highlighted the relevancy of nurses in the detection of AF, not only by manual palpation but also by using new eHealth tools.33-35 Their role in educating about AF is also key, given that many patients report difficulties understanding what AF is, why they have to be treated with anticoagulation, and why this therapy is usually a lifelong treatment. Thus, nurses contribute to better tailored patient AF-related education.36

Regarding the impact of nurse-led models of care over clinical outcomes, there are limited studies and do not provide conclusive evidence. A recent randomized clinical trial failed to show that nurse-led care was superior to usual-care reducing the composite of cardiovascular death and cardiovascular hospital admissions.37 Similarly, the NEAT study showed that a nurse-delivered educational intervention did not significantly impact on health-related quality of life or risk factor status in individuals with AF.38 However, adherence to guideline recommendations is higher when nurses are involved in the AF clinic and this could be related with better clinical outcomes.39 For example, a recent retrospective study found that the management of AF in a nurse-led clinic was associated with high level of adherence to anticoagulation guidelines.40 Also, an integrated specialized nurse-driven, physician supervised AF clinic demonstrated to reduce all-cause mortality compared with usual care.41 A randomized clinical trial also demonstrated that nurse-led care of patients with AF is superior to routine clinical care, reducing the risk of cardiovascular death (HR 0.28; 95% CI 0.09-0.85, p=0.025) and cardiovascular hospitalization (HR 0.66; 95% CI: 0.46-0.96, p=0.029).42 This has been proposed in other studies where nurse-led clinics showed to contribute on sustained follow-up care, preventing hospitalizations, improving outcomes, reducing AF burden through lifestyle modification and addressing current deficiencies in AF management.43-45 Furthermore, an ongoing trial aims to assess the effect of nurse practitioner-led care on the health-related quality of life in patients with AF, as well as to measure its impact on relevant outcomes such as death, hospitalization, and emergency department visits.46 Recent systematic reviews and meta-analyses shown that, in overall, nurse-led clinics improved healthcare, patient and quality care outcomes. Mortality rates and cardiovascular hospitalisations are lower, whereas patient medication adherence, quality of life and guideline adherence are higher in nurse-led AF clinics compared to usual care.47,48 The results of our study seem to reinforce the hypotheses of better clinical outcomes in a specific AF clinic led by nurses, since the rate of ischemic stroke/TIA was significantly lower in the group of patients followed-up in this clinic. 28-32

For the above reasons, AF management models including nurses within the healthcare team or nurse-coordinated AF programmes are highly encouraged.49 A report from the PINNACLE registry concluded that a collaborative care model, using both physicians and nurses, may provide an overall comparable quality of outpatient cardiovascular care compared with a physician-only model.50 However, there is available evidence showing that a multi-disciplinary healthcare team constituted of primary care providers (physicians [including cardiologists, arrhythmologists, general practitioners and other specialists], physician assistants, and nurse practitioners), nurses, and pharmacists can provide improved medical management for stroke prevention in AF patients.51 Furthermore, a structured AF management within an integrated care approach should include some core components such as: a) patient-centeredness; b) multidisciplinary team; c) use of smart technology; and d) application of a comprehensive approach to care with access to all treatment options.39 Indeed, the ESC guidelines for the management of AF suggest that patients need regular follow-up undertaken by specially trained nurses, cardiologists, or AF specialists.10

*Limitations*

There are some limitations that we should acknowledge. This study is limited by its observational nature and a single centre design with Caucasian based population. Of note, our study was performed with patients initially taking VKA, not DOACs, thus our results cannot be translated to that population. There are still restrictions in Spain to DOAC prescription, and all naïve AF patients have to start OAC therapy with VKAs. Therefore, all of our patients included in the nurse-led AF clinic were taking this therapy and for the same reason we only included patients taking VKAs in the usual care group, to allow comparisons. In addition, this study was purposed as a pilot study and a power calculation for the endpoints was not performed. Thus, new prospective studies or clinical trials are needed to validate our results. Finally, these results should be interpreted with caution as they are not necessarily generalizable to other different healthcare settings and should be regarded as hypothesis-generating.

**Conclusion**

The present study shows that a nurse-led clinic including patients newly diagnosed with AF and starting OAC therapy with VKAs, may offer a more ‘patient-centered’ review and follow-up, and it would be associated with a reduction of ischemic stroke/TIA events, without an increase in bleeding complications. This study should be considered as hypothesis-generating and further studies are warranted to confirm these results.

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**Table 1.** Baseline characteristics.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Overall**  **N = 223** | **Nurse-led clinic**  **N = 107** | **Usual care**  **N = 116** | **p-value** |
| **Demographic** |  |  |  |  |
| Age (years), median (IQR) | 75 (68-81) | 72.5 (64-80) | 76.5 (70-82) | 0.005 |
| Age ≥60 years, n (%) | 204 (91.9) | 94 (88.7) | 110 (94.8) | 0.094 |
| Male sex, n (%) | 121 (54.5) | 58 (54.7) | 63 (54.3) | 0.952 |
|  | | | | |
| **Comorbidities, n (%)** |  |  |  |  |
| Hypertension | 176 (79.3) | 85 (79.4) | 91 (79.1) | 0.955 |
| Diabetes mellitus | 95 (42.8) | 41 (38.3) | 54 (47.0) | 0.194 |
| Hyperlipemia | 106 (47.7) | 51 (47.7) | 55 (47.8) | 0.981 |
| Coronary artery disease | 78 (35.0) | 39 (36.4) | 39 (33.6) | 0.658 |
| Heart failure | 94 (42.2) | 42 (39.3) | 52 (44.8) | 0.400 |
| Peripheral artery disease | 21 (9.4) | 13 (12.1) | 8 (6.9) | 0.180 |
| Stroke/TIA/thromboembolism | 31 (13.9) | 12 (11.2) | 19 (16.4) | 0.265 |
| OSA/COPD | 47 (21.1) | 24 (22.4) | 23 (19.8) | 0.634 |
| Renal impairment | 93 (41.7) | 44 (41.1) | 49 (42.2) | 0.865 |
| Hepatic impairment | 7 (3.2) | 4 (3.7) | 3 (2.6) | 0.630 |
| Thyroid dysfunction | 20 (9.0) | 5 (4.7) | 15 (12.9) | 0.031 |
| Tobacco use | 76 (34.2) | 44 (41.1) | 32 (27.8) | 0.037 |
|  | | | | |
| **Concomitant treatment, n (%)** |  |  |  |  |
| Antiarrythmics | 32 (14.3) | 15 (14.0) | 17 (14.7) | 0.892 |
| Calcium channel blockers | 50 (22.4) | 22 (20.6) | 28 (24.1) | 0.522 |
| Beta-blockers | 155 (70.1) | 83 (77.6) | 72 (63.2) | 0.019 |
| Statins | 133 (59.6) | 64 (59.8) | 69 (59.5) | 0.960 |
| Diuretics | 42 (18.8) | 16 (15.0) | 26 (22.4) | 0.155 |
| Antiplatelet therapy | 65 (29.1) | 38 (35.5) | 27 (23.3) | 0.045 |
| ACEIs/ARBs | 161 (72.2) | 79 (73.8) | 82 (70.7) | 0.601 |
|  | | | | |
| CHA2DS2-VASc, median (IQR) | 4 (3-5) | 4 (2-5) | 4 (3-5) | 0.022 |
| CHA2DS2-VASc ≥2 | 208 (93.3) | 98 (91.6) | 110 (94.8) | 0.355 |
| HAS-BLED, median (IQR) | 3 (2-4) | 3 (2-3) | 3 (2.3-4) | <0.001 |
| HAS-BLED ≥3 | 141 (63.2) | 54 (50.5) | 87 (75.0) | <0.001 |
| ACEIs/ARBs = Angiotensin-converting enzyme inhibitors/Angiotensin receptor blockers; CHA2DS2-VASc = cardiac failure or dysfunction, hypertension, age ≥75 [doubled], diabetes, stroke [doubled] – vascular disease, age 65-74 yr and sex category [female]; HAS-BLED = hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly, drugs/alcohol concomitantly age; IQR = interquartile range; OSA/COPD = obstructive sleep apnea/Chronic obstructive pulmonary disease; TIA = transient ischemic attack. | | | | |

**Table 2.** Factors associated with poor quality of anticoagulation (i.e. TTR <65%) by logistic regression analyses.

|  |  |  |
| --- | --- | --- |
|  | **Univariate analysis**  **OR (95% CI), p-value** | **Multivariate analysis**  **OR (95% CI), p-value** |
| Age | 1.02 (0.99-1.05), 0.153 | - |
| Male sex | 1.40 (0.78-2.51), 0.258 | - |
| Hypertension | 1.25 (0.62-2.54), 0.537 | - |
| Diabetes mellitus | 1.41 (0.78-2.56), 0.255 | - |
| Hyperlipemia | 0.91 (0.51-1.63), 0.748 | - |
| Coronary artery disease | 1.21 (0.65-2.24), 0.548 | - |
| Heart failure | 1.02 (0.57-1.83), 0.953 | - |
| Peripheral artery disease | 1.05 (0.39-2.87), 0.920 |  |
| Stroke/TIA/thromboembolism | 1.95 (0.76-5.03), 0.166 | - |
| OSA/COPD | 2.35 (1.03-5.39), 0.043 | 2.06 (0.88-4.83), 0.095 |
| Renal impairment | 0.93 (0.52-1.67), 0.810 | - |
| Hepatic impairment | 2.29 (0.26-19.98), 0.454 | - |
| Thyroid dysfunction | 0.75 (0.28-2.00), 0.564 |  |
| Tobacco use | 0.80 (0.43-1.46), 0.458 | - |
| Antiarrythmics | 1.08 (0.45-2.60), 0.870 | - |
| SAMe-TT2R2 | 0.91 (0.69-1.19), 0.484 | - |
| CHA2DS2-VASc | 1.15 (0.96-1.38), 0.127 | 1.00 (0.79-1.25), 0.964 |
| HAS-BLED | 1.48 (1.14-1.93), 0.003 | 1.45 (1.05-2.02), 0.026 |
| OSA/COPD = obstructive sleep apnea/Chronic obstructive pulmonary disease; OR = odds ratio; TIA = transient ischemic attack. | | |

**Table 3.** Comparison of adverse events and annual event rates.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Event** | **Overall**  **n (%)** | **Nurse-led AF Clinic (N = 107)** | | **Usual care (N = 116)** | | | **p-value** |
| **n (%)** | **Annual event rate (%/year)** | | **n (%)** | **Annual event rate (%/year)** |
| ***Efficacy endpoints*** | | | | | | | |
| Ischemic stroke/TIA | 10 (4.48) | 1 (0.93) | 0.47 | | 9 (7.75) | 3.88 | 0.016 |
| Acute myocardial infarction | 8 (3.59) | 2 (1.87) | 0.94 | | 6 (5.17) | 2.59 | 0.193 |
| Mortality | 49 (21.97) | 22 (20.56) | 10.28 | | 27 (23.27) | 11.64 | 0.666 |
| ***Safety endpoints*** | | | | | | | |
| Major bleeding | 25 (11.21) | 9 (8.41) | 4.21 | | 16 (13.79) | 6.90 | 0.231 |
| CRNMB | 48 (21.52) | 27 (25.23) | 12.62 | | 21 (18.10) | 9.05 | 0.252 |
| Any bleeding | 64 (28.70) | 32 (29.90) | 14.95 | | 32 (27.59) | 13.79 | 0.747 |
|  | | | | | | | |
| CRNMB = clinically relevant non-major bleeding; TIA = transient ischemic attack. | | | | | | | |

**Figure 1.** Cumulative incidence of ischemic stroke/transient ischemic attack.

Figure 1.tif