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Assessment of Oral Anticoagulation with Vitamin K Antagonists in Patients Living in a Low-Income Country of West Africa

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Abstract

Introduction: Despite the rise of direct oral anticoagulants (DOACs), vitamin K antagonists (VKA) remain the most widely used oral anticoagulants in developing countries. The aim of this study was to estimate the prevalence of good anticoagulation in patients treated with VKA in Lomé and describe associated factors. **Methods:** This was a cross-sectional study conducted from November 2019 to October 2020 in the cardiology departments of two University teaching hospitals in Lomé (CHU Sylvanus Olympio and CHU Campus), involving patients on VKA for ≥3 months, with a target international normalized ratio (INR) of 2.5 and a therapeutic margin between 2 and 3. The quality of anticoagulation was assessed by the *time in therapeutic range* (TTR) which was assessed by the Rosendaal method. Good anticoagulation was defined by a TTR > 70%. **Results:** A total of 344 patients were included (mean age = 58 ± 13.8 years, women = 56.1%). Indications for VKA treatment were represented by venous thromboembolic disease (43.3%), supraventricular arrhythmia (28.2%), severe left ventricular systolic dysfunction (19.8%) and pulmonary hypertension (8.7%). The average TTR was 47.6 ± 20.8%. The rate of good anticoagulation was 17.7%. Factors associated with good anticoagulation were the use of fluindione vs acenocoumarol (OR = 11.17; 95% CI: 3.2 - 39.6; p = 0.0002), concomitant low-dose aspirin (OR 4.44; 95% CI: 1.4 - 13.9; p = 0.01) and INR monitoring exclusively by the patient himself (OR = 4.92; 95% CI: 1.5 - 16.3; p = 0.008). The rate of thromboembolic and hemorrhagic complications was each 2.6% and was not correlated with the quality of anticoagulation. Quality of anticoagulation by VKAs was poor in our practice. Factors associated with good anticoagulation were the use of fluindione vs acenocoumarol, concomitant low-dose aspirin and mon-

itoring of INR exclusively by the patient himself. **Conclusion:** The quality of oral anticoagulation by VKAs could be improved in our practice by the creation of anticoagulation clinics for better therapeutic education of patients and efficient management of VKA dose, and the use of prescription assistance software.

Keywords

Vitamin K Antagonists, *Time in Therapeutic Range*, Lomé, Togo

1. Introduction

Anticoagulants are commonly used in medicine in the prevention and treatment of thromboembolic diseases [1] [2] [3] and vitamin K antagonists (VKAs) were the only oral anticoagulants available for decades. However, VKAs have a narrow therapeutic index and require regular monitoring of their anticoagulant activity, which involves measuring the Prothrombin Time, expressed in international normalized ratio (INR) [4]. Since the availability of direct oral anticoagulants (DOACs), the use of VKAs is experiencing a sharp decline at the expense of the former, even if they remain the oral anticoagulants of choice in some indications such as atrial fibrillation associated with mitral stenosis or mechanical valve prosthesis [5]. Indeed, DOACs are immediately active, not necessarily requiring prior use of heparin [6]; they do not require monitoring of their anticoagulant activity, which exempts patients from repetitive blood sampling and they do not present food interactions [7]. Furthermore, they would be safer than VKAs with regard to bleeding complications [8] [9] [10] [11].

But in low and middle-income countries, such as Togo, it is a challenge to obtain DOACs due to their high cost compared to the standard of living of the populations and their lack of availability in pharmacies. In these countries, VKAs remain widely used.

The time in therapeutic range (TTR) estimates the percentage of time a patient's INR is within the desired range. It evaluates the quality of VKA treatment and constitutes an important tool for evaluating the benefit-risk ratio [12]. A TTR > 70% indicates good anticoagulation [13] even if in the literature, a threshold of 65% is sometimes found [14] [15]. Several Western studies have evaluated the quality of oral anticoagulation by VKA using TTR. Anticoagulation was generally of poor quality [16] [17] [18] [19] as well as in the scares African studies on this topic [15] [20] [21]. In Togo, we did not find any data on this subject, hence the interest of the present study. The objective of the present study was to evaluate the quality of anticoagulation by VKA in Lomé, using TTR, and describe associated factors.

2. Materials and Methods

This study was carried out in the cardiology departments of two University

teaching hospital (CHU Sylvanus Olympio and CHU Campus) in Lomé, Togo. This was a cross-sectional study with descriptive and analytical aims, carried out from November 2019 to October 2020.

2.1. Inclusion Criteria

This study focused on patients undergoing anticoagulant treatment with VKA, followed up on outpatient basis, whatever the indication for anticoagulant treatment. Inclusion has been done consecutively in patients aged 18 years or more, with a therapeutic INR range between 2 and 3 therefore a target INR of 2.5, who are taking VKAs for at least three months, and who routinely checked their INR levels, to allow the calculation of TTR: at least one INR per month and at least six INRs in total at the end of the study.

2.2. Non-Inclusion Criteria

Patients who did not have an INR monitoring log book and those who had not given their consent were excluded from this study.

2.3. Sample Size Calculation

Considering a hospital VKA prescription rate of 27.6% [21], a margin of error of 5% and a confidence level of 95%, the minimum sample size was 308 patients when applying Schwartz's formula [22]:

$$n = t^2 \times p \times (1-p) / m^2$$

(with n = minimum sample size to obtain significant results for an event and a fixed risk level, t = confidence level (the typical value of the 95% confidence level will be 1.96), p = proportion estimate of the population which presents the characteristic and m = margin of error). Anticipating a non-response rate of 10%, we needed to include at least 339 patients.

2.4. Data Collection

Data were collected on an individual survey form by crossing two sources: the questioning of the patients themselves or of their companions in the event of cognitive disorder or their unavailability and the INR monitoring logbook. The following data were collected prospectively:

- Epidemiological and clinical variables: age, gender, place of residence (urban or rural), level of education, degree of autonomy assessed by the modified MMS score [23] [24], indication of VKA, comorbidities, type of VKA, duration of VKA treatment, concomitant medications and their number;
- Monitoring of INR: delivery of INR results to the hospital and receipt of instructions relating to the dosage of VKA which could be done by the patient himself or a companion in the event of the latter's unavailability;
- The TTR was calculated for each patient with a computer program in Excel format, using the Rosendaal method [25]. A TTR > 70% was considered to indicate good anticoagulation;

- Thromboembolic complications: any thrombotic and/or embolic event occurring during treatment with VKA such as pulmonary embolism, ischemic stroke, venous thrombosis;
- Hemorrhagic complications: minor and major hemorrhage was defined, according to the criteria of the International Society on Thrombosis and Haemostasis [26].

2.5. Data Analysis

Categorical variables are expressed as counts and percentages and comparisons were made using the Chi-square test or Fisher's exact test. Continuous variables are expressed as means and standard deviations (SDs) or medians and interquartile ranges (IQRs) and comparisons were made with Student's t test or the Mann-Whitney U test.

Univariate logistic regression was performed between the TTR > 70% (dependent variable) and the covariates which were the epidemiological, clinical and therapeutic data (age ≥ 60 years [27], gender, urban or rural place of residence, level of education, comorbidities, degree of autonomy of patients, length of VKA treatment ≥ 1 year, monitoring of INR exclusively by the patient himself, the VKA molecules used, the number of drugs including the VKA ≥ 3).

Multiple logistic regression analyses were performed after adjustments (with covariates which showed $p \leq 0.25$ in univariate analysis). Odds ratios (OR) were expressed with their 95% confidence interval (95% CI). For all tests, statistical significance was set at $p < 0.05$. The data were analyzed using EPI INFO software version 7.2.1.0.

3. Results

3.1. Epidemiological and Clinical Characteristics of the Study Population

Overall, 344 patients were included: 189 (54.9%) patients at the CHU Campus and 155 (45.1%) patients at the CHU Sylvanus Olympio. This sample included 151 (43.9%) men and 193 (56.1%) women. The mean age was 57.9 ± 13.7 years (range = 20 and 89 years) with no gender difference (men: 57.8 ± 12.2 years versus 57.9 ± 14.8 years in women; $p = 0.91$). Patients residing in urban areas that 326 (94.8%) and 84 (24.4%) had university education level. Total autonomous patients numbered 310 (90.1%). The main indications for VKA treatment were venous thromboembolism 149 (43.3%) and non-valvular atrial fibrillation 97 (28.2%) (**Table 1**).

3.2. Vitamin K Antagonist Treatment and Associated Medications

Fluindione was prescribed to 246 (71.5%) patients and acenocoumarol to 95 (27.6%) patients. Loop diuretics were prescribed in combination with VKA in 173 (50.3%) patients and low-dose aspirin to 30 (8.7%) patients. Mean number of medications per patient was 3.5 ± 2.1. Patients who only took VKA as their medication were 79 (23%) (**Table 2**).

Table 1. Epidemiological clinical characteristics of the study population.

Variables	n	%
Female	193	56.1
Residence		
Urban	326	94.8
Rural environment	18	5.2
Level of education		
University level	84	24.4
Secondary school	109	31.7
Primary school	108	31.4
Unschooled	44	12.5
Patient's autonomy		
Total autonomous patients	309	89.8
Partially dependents patients	32	9.3
Dependents patients	3	0.9
Indications for vitamin K antagonists		
Venous thromboembolism	149	43.3
Supraventricular rhythm disturbances	97	28.2
Severe left ventricular systolic dysfunction	68	19.8
Pulmonary hypertension	30	8.7
Comorbidities		
Heart failure	115	33.4
High blood pressure	92	26.7
Stroke	30	8.7
Cancer	18	5.2
Diabetes	18	5.2
Chronic renal failure	15	4.4
HIV immunosuppression	6	1.7

HIV: Human Immunodeficiency Virus.

Table 2. Vitamin K antagonists and co-prescribed medications.

Variables	n	%
Type of VKA molecules		
Fluindione	246	71.5
Acenocoumarol	95	27.6
Warfarin	3	0.9

Continued

Concomitant medications		
Loop diuretics	173	50.3
Beta-blockers	159	46.2
ACE inhibitors	158	45.9
Spironolactone	151	43.9
Proton pump inhibitors	67	19.5
Amlodipine	34	9.9
Low-dose aspirin	30	8.7
Atorvastatin	21	6.1
Digoxin	18	5.2
Angiotensin 2 receptor antagonists	15	4.4
Corticosteroids	11	3.2
Oral antidiabetics	10	2.7
Insulin	8	2.3
Amiodarone	3	2.8

3.3. INR Monitoring

In this sample, 241 (70.1%) patients exclusively monitored INR themselves. INR monitoring was mixed (sometimes the patient, sometimes an individual close to him) in 21 (6.1%) patients; it was provided exclusively by accompanying persons in 82 (23.8%) patients when the patients were not independent or were unavailable.

3.4. Duration of VKA Treatment

The cumulative number of days spent on VKA by all patients was 95,751 days. Mean time spent on VKA per patient was 279 ± 179.7 days.

3.5. Efficacy of Anticoagulant Treatment

Overall, 5705 INR measurements were analyzed. Mean number of INRs performed per patient was 16.6 ± 7.8. Mean duration between 2 INR checks was 18.5 ± 8.3 days. The percentage of INR between 2 and 3 was 38% (2168/5705).

Mean TTR was 47.6 ± 20.8%; 61/344 (17.7%) patients had good anticoagulation (TTR > 70%) and 283/344 (82.3%) patients had poor level of anticoagulation (TTR ≤ 70%). On average, the percentage of time spent below the therapeutic margin per patient was 34% ± 21% and the mean percentage of time spent above the therapeutic margin was 17% ± 16.2%.

3.6. Factors Associated with the Quality of Anticoagulation

There was a positive correlation between TTR > 70% and the following factors:

age < 60 years (OR = 2.44; 95% CI 1.34 - 4.43; p = 0.003), being male (OR = 1.78; 95% CI 1.02 - 3.12; p = 0.04), INR monitoring exclusively by the patient himself (OR = 2.91; 95% CI 1.37 - 6.17; p = 0.005), use of fluindione (OR = 7.08; 95% CI 2.49 - 20.1; p = 0.002), concomitant use of low-dose aspirin (OR = 3.60; 95% CI 1.63 - 7.95; p = 0.001), and proton pump inhibitors (OR = 1.95; 95% CI 1.03 - 3.6; p = 0.03); while a negative correlation was observed with factors such as concomitant use of beta-blockers (OR = 0.55; 95% CI 0.30 - 0.98; p = 0.04), ACE inhibitors (OR = 0.55; 95% CI 0.31 - 0.99; p = 0.04), and a number of medications ≥ 3 (OR = 0.49; 95% CI 0.28 - 0.85; p = 0.01) (Table 3).

After adjustments, a positive correlation persisted between TTR > 70% and the following factors: use of fluindione (adjusted OR = 11.17; 95% CI 3.15 - 39.57; p = 0.0002), concomitant low-dose aspirin (adjusted OR = 4.44; 95% CI 1.42 - 13.9; p = 0.01) and the monitoring of INR exclusively by the patient himself (adjusted OR = 4.92; 95% CI 1.49 - 16.24; p = 0.008) (Table 4).

Table 3. Univariate logistic regressions between anticoagulation quality and covariates.

	Total n = 344	TTR ≤ 70% n = 283	TTR > 70% n = 61	OR	95%CI	p
Age < 60 years	183 (53.2)	140 (49.5)	43 (70.5)	2.44	1.34 - 4.43	0.003
Male	151 (43.9)	117 (41.34)	34 (55.74)	1.78	1.02 - 3.12	0.04
Urban residence	326 (94.8)	268 (94.7)	58 (95.1)	1.08	0.30 - 3.84	0.90
University level	84 (24.4)	68 (24.3)	16 (26.2)	1.12	0.59 - 2.11	0.71
Total autonomy	309 (89.8)	251 (88.7)	58 (95.1)	2.46	0.72 - 8.32	0.14
INR monitoring by the patient himself	240 (69.8)	188 (66.4)	52 (85.3)	2.91	1.37 - 6.17	0.005
High blood pressure	92 (26.7)	80 (28.3)	12 (19.7)	0.62	0.31 - 1.23	0.17
Diabetes	18 (5.2)	15 (5.3)	3 (4.9)	0.92	0.25 - 3.29	0.90
Obesity	9 (2.6)	6 (2.1)	3 (4.2)	2.38	0.58 - 9.82	0.22
Heart failure	115 (33.4)	97 (34.3)	18 (29.5)	0.80	0.43 - 1.46	0.47
Fluindione	246 (71.5)	189 (66.8)	57 (93.4)	7.08	2.49 - 20.1	0.0002
≥3 medications	202 (58.7)	175 (61.8)	27 (4.3)	175	0.28 - 0.85	0.01
Loop diuretics	173 (50.3)	146 (51.6)	27 (44.3)	0.74	0.42 - 1.29	0.30
Spironolactone	151 (43.9)	130 (45.9)	21 (34.4)	0.61	0.34 - 10	0.10
Beta blockers	159 (46.2)	138 (48.8)	21 (34.4)	0.55	0.30 - 0.98	0.04
ACE inhibitors	158 (45.9)	137 (48.4)	21 (34.4)	0.55	0.31 - 0.99	0.04
Digoxin	18 (5.2)	12 (4.2)	6 (9.8)	2.46	0.88 - 6.84	0.08
Proton pump inhibitors	68 (19.8)	50 (17.7)	18 (29.5)	1.95	1.03 - 3.66	0.03
Low-dose aspirin	30 (8.7)	18 (6.4)	12 (19.7)	3.60	1.63 - 7.95	0.001
≥365 days of anticoagulation	271 (78.8)	223 (78.8)	48 (78.7)	1.00	0.51 - 1.97	0.98

OR: Odd Ratio; 95% CI: 95% Confidence Interval.

Table 4. Multivariate logistic regressions between the quality of anticoagulation (TTR > 70%) and the covariates.

Variables	Adjusted OR	95%CI	Adjusted p
Fluindione	11.17	3.15 - 39.57	0.0002
Low-dose aspirin	4.44	1.42 - 13.90	0.01
Age < 60 years	1.39	0.61 - 3.15	0.42
Monitoring of INR exclusively by the patient himself	4.92	1.49 - 16.24	0.008
≥3 medications	0.52	0.14 - 1.84	0.31
Proton pump inhibitors	1.79	0.71 - 4.52	0.21
Male	1.71	0.87 - 3.36	0.11
Beta blockers	0.48	0.12 - 1.82	0.28
ACE inhibitors	1.43	0.31 - 6.64	0.64

OR: Odd Ratio; 95% CI: 95% Confidence Interval.

3.7. Ischemic and Hemorrhagic Outcomes

Nine of the 344 patients (2.6%) had thromboembolic complications. The rate of thromboembolic complications seemed higher in patients with effective anticoagulation without significant difference: 3/61 (4.9%) versus 6/283 (2.12%); OR = 2.4; 95% CI [0.58 - 9.83]; p = 0.23.

Hemorrhagic complications were found in 9/344 patients (2.6%). All 9 (100%) patients had a TTR ≤ 70% and none (0%) of them had a TTR > 70% (p = 0.97). Concomitant low-dose aspirin was correlated with the occurrence of hemorrhagic complications with 3/30 (30%) patients compared to 6/314 (1.9%) in the group of patients without low-dose aspirin (OR = 5.70; 95% CI = 1.4 - 24.1; p = 0.02).

4. Discussion

In this sample of patients undergoing VKA treatment living in a low-income country of West African, we assessed the quality of anticoagulation using the TTR. Mean TTR was 47.6% ± 20.8%. The rate of good anticoagulation (TTR > 70%) was 17.7%. After multivariate logistic regression analysis, three variables were statistically associated with good anticoagulation: use of fluindione, concomitant low-dose aspirin and the monitoring of INR exclusively by the patient himself.

Quality of anticoagulation was generally poor in this study. This pattern of poor anticoagulation has also been observed in Cote d'Ivoire [20] and Tunisia [28] and in South Africa [29] where the rates of good anticoagulation defined by a TTR ≥ 65% were respectively 11%, 22% and 25.1%. These results from African studies are below those observed in Europe. Indeed, Cotté *et al.* observed that the proportion of patients with atrial fibrillation on VKA and having

a TTR > 70% was 47.8% in France, 44.2% in Germany, 46.1% in Italy and 65.4% in the United Kingdom [19]. *i.e.*, a rate of good anticoagulation 2 or 3 times higher than those observed in Africa. Even if these results from European studies were better than those observed in our study, it must be emphasized that anticoagulation by VKA was also of poor quality in these countries. The poor quality of oral anticoagulation by VKA in our area can be explained by the lack of therapeutic education of patients [30]. Therapeutic education can be improved by anticoagulation clinics which are services dedicated to the therapeutic education of patients as well as the collection of INRs and the adjustment of VKA dosages. Use of prescription assistance software in anticoagulation clinics has also demonstrated its effectiveness in this study [31] [32]. Based on the INR results, such software automatically suggests the VKA drug management including drug dosage and the date of next INR: they thus help to limit the risk of error on the part of the nursing staff. Other factors such as genetic variability and dietary interference may also explain the difficulty in having effective anticoagulation thresholds by VKA [20].

INR monitoring performed exclusively by the patient himself without intervention of a companion favored good anticoagulation in this study. The intervention of companions can lead to an alteration of the messages sent by the doctor or the nurse to the patient. When presenting INR results the patient who monitors his INR can directly ask the doctor questions regarding his treatment. These discussions can be an opportunity to evaluate the patient's level of knowledge regarding VKA treatment as well as the related measures. Such visit may be an occasion to remind him about taking medications and foods which can unbalance the INR. Monitoring of INRs by patients themselves should be encouraged whenever possible.

Patients treated with fluindione had better anticoagulation than those treated with acenocoumarol. This may be explained by the fact that fluindione has a longer half-life than acenocoumarol. Indeed, it has been reported that the longer the half-life of VKA is, the more it guarantees better stability of the INR [33].

Concomitant use of low-dose aspirin was associated with good anticoagulation in the present study even if it also increased the risk of bleeding. This may be explained by the fact that low-dose aspirin potentiates the anticoagulant action of VKA [4].

Mean number of medications in our patients was 3.5 ± 2. A number of medications greater than or equal to 3 was associated with poor anticoagulation in univariate analysis but this association did not persist after adjustments. Such threshold was higher in Iran where Farsad *et al.* [14] reported increased risk of poor anticoagulation with a number of medications ≥ 5 (OR = 2.06; 95% CI, 1.87 - 2.23). It was reported that polypharmacy can be a factor in poor anticoagulation due to interactions between VKAs and some medications [4]. It is therefore necessary to take into account the pharmacological properties of any medication before prescribing it in combination with a VKA drug since it

can modify the INR [4].

5. Limitations

The Rosendaal method which was used to calculate the TTR has certain limitations. First, it uses interpolation which is a mathematical operation allowing a curve to be constructed from a finite number of values; for the calculation of the TTR, the interpolation is assumed to be linear, but the changes in the INR are not necessarily linear. Then, the TTR is very sensitive to the frequency of the INRs, but the delay between the different INRs carried out in this study was not uniform. Second, the TTR is indifferent to large variations in INR values: the risk of immediate hemorrhagic complications may thus be underestimated [28].

Another limitation of this study was the impossibility of assessing complications in real time and objectively, particularly hemorrhagic complications. This could explain their relatively low rate; then minor hemorrhages may have been trivialized or forgotten by patients. Additionally, for patients who did not monitor INR themselves, information was collected by hetero anamnesis, which could represent recruitment bias.

6. Conclusion

Quality of oral anticoagulation by VKAs was poor in our practice. Factors associated with good anticoagulation were the use of fluindione (vs acenocoumarol), concomitant low-dose aspirin and monitoring of INR exclusively by the patient himself. The quality of oral anticoagulation by VKAs could be improved in our practice by the creation of anticoagulation clinics for better therapeutic education of patients and efficient management of VKAs dose, and the use of prescription assistance software. Weak anticoagulation quality of VKAs could justify an expansion of the prescription of DOACs if they are available and accessible.

Authors' Contributions

KY: designed the study, wrote the protocol and corrected the manuscript;
TT, EHL: managed analysis and discussion and corrected the manuscript;
APD, ET, MK, EHL: managed the literature searches;
AA, SP, SB, and DF: managed data collection.

Conflicts of Interest

The authors declare that they have no competing interests.

Ethical Considerations

Ethical approval was obtained from the Institutional Review Board of the Faculty Health Sciences of the University of Lomé (Togo). We also obtained administrative approval from the General Managers of the two hospitals. Oral consent has been obtained for each patient. For the purpose of confidentiality, participant's

data were processed using specific unique identifiers.

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Appendix

Individual Survey Form

Assessment of oral anticoagulation with vitamin K antagonist (VKA) in patients living in a low-income century of West Africa.

Study center: /……../ University Teaching Hospital Campus [1]; University Teaching Hospital Sylvanus Olympio [2]

PATIENTS Id

- **Last name + first name** (initials): ……
- **Age:** ……years
- **gender:** ……. □M [1] □F [2]
- **contact:** …….
- **Occupation:** /…../

□civil servant/employee [1] □individual [2] □artisan [3] □housewife [4] □retired [5] □other [6]: specify if other: ……

- **Patient's education level:** /……../

Not in school [1] primary [2] secondary [3] higher [4]

- **Educational level accompaniment** if non-autonomous or unavailable patient: /……../

Not in school [1] primary [2] secondary [3] higher [4]

- **Residence:** /……/

Lomé [1] other city [2] rural [3] other [4]: specify if other……..

- **Ethnicity:** ……...……
- **Blood group-Rhesus factor:** /……./

HISTORY /…….…….. / (Many possible responses)

None [1] -stroke [2] -hypertension [3] -diabetes [4] -obesity [5] -dyslipidemia [6] -alcohol [7] -tobacco [8] -heredity [9] -menopause [10] -heart failure [11] -cardiopathy [12] …… -hepatopathy [13] …….. -Hepatocellular insufficiency [14] -renal insufficiency [15]; GFR (MDRD) …….. nephropathy [16] ……..-hemopathy [17] …… -neuropathy [18] ……. -neoplasia [19] …….. -HIV [20] -asthma [21] -sickle cell disease [22] -hyperthyroidism [23] -hypothyroidism [24] -Pulmonary embolism [25] -Deep vein thrombosis [26] -severe pulmonary hypertension [27] -Other [28]; specify if other ……

Cognitive Functions: /……/

autonomous [1] semi-autonomous [2] dependent [3]

Indication for VKA treatment: /……..…/

Deep vein thrombosis [1]; Pulmonary embolism [2]; Deep vein thrombosis + Pulmonary embolism [3]; recurrence of venous thromboembolic disease [4]; severe pulmonary hypertension [5]; non-valvular atrial fibrillation [6]; valvular atrial fibrillation [7]; severe left ventricular dysfunction [8]; mechanical valve prosthesis [9]; or bioprosthesis [10]; other [11]; specify other: …….

VKA molecule: /…….……/

Acenocoumarol (SINTROM) [1]; Fluindione (previscan) [2]; Warfarin (coumadin) [3]; other [4]; specify if other…….

Change of VKA molecule: /……..…/

Yes [1] no [2]

If yes, specify reason: /……../

Outage on market [1]; inefficacy [2]; other [3]: ……

Expected duration of treatment with VKA: /……..…/

3 months **[1]**; 6 months **[2]**; long term/indeterminate **[3]**; for life **[4]**

Total number of patient's medications: including VKA: /……../

Molecules co-prescribed in association with VKA: /……../

Furosemide [1]; spironolactone [2]; bisoprolol [3]; nebivolol [4]; metoprolol [5]; propanolol [6]; other beta-blocker [7]; perindopril [8]; rampipril [9]; enalapril [10]; ACE inhibitor [11]; ARB [12]; digoxin [13]; amiodarone [14]; neomercazole [15]; omeprazole [16]; lansoprazole [17]; rabeprazole [18]; pantoprazole [19]; aspirin [20]; others [21] …….

Baseline prothrombin time …… or **spontaneous INR …….**

INR TABLE

Date	INR	Dosage	Incident/accident

Continued

Results:

Time spent under VKA: ……..…….. Days

Total number of INR performed: …….

Percentage of INR between 2 and 3: ……

Number of days in the effectiveness zone: …….

TTR according to the Rosendaal method: ……..%

Percentage of time spent below the therapeutic range: ……%

Percentage of time spent above the therapeutic margin: ……%

Thromboembolic outcomes: /……../

if yes specify: ……

Hemorrhagic outcomes: /……../

if yes specify:……

Evolution of the outcomes: /……/

favorable [1], death [2], other [3] ……..