

# Evaluation of Anticoagulation therapy in non-valvular Atrial Fibrillation in the emergency department

## Evaluation de la prescription des Anti-vitamines K au cours de la fibrillation auriculaire non valvulaire aux Urgences

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### R É S U M É

**Introduction:** Les anti-vitamines K (AVK) sont actuellement la classe thérapeutique la plus prescrite pour la prévention des accidents vasculaires cérébraux chez les patients en fibrillation auriculaire non valvulaire (FANV). En dépit de leur efficacité démontrée, les AVK sont sous-utilisés chez les patients à haut risque thromboembolique.

L'objectif de ce travail était d'évaluer la prescription des AVK chez les patients en FANV et les facteurs associés à une sous-prescription.

**Méthode :** Etude prospective, observationnelle, menée dans un service des urgences. Inclusion : patients avec FANV à haut risque thromboembolique et qui ne sont pas sous AVK. Calcul du CHA2DS2-VASc et HASBLED scores. Une étude analytique a été faite afin de connaître les facteurs indépendamment associés à la non prescription des AVK.

**Résultats :** Inclusion de 176 patients. Age moyen=  $67 \pm 13$  ans. Sex-ratio=0,5. Score CHA2DS2VASc moyen=  $2,88 \pm 1,55$  et score HASBLED moyen=  $1,52 \pm 1,05$ . Les AVK ont été prescrits dans 36% des cas. En analyse multivariée, l'âge  $\geq 70$  ans (ORajusté =1,59 ; IC 95% [1,11-2,21];  $p < 0,001$ ), une créatininémie  $\geq 110 \mu\text{mol/l}$  (ORajusté =2,54; IC 95% [1,20-5,37];  $p = 0,01$ ) et la prise d'aspirine (ORajusté=1,7; IC 95% [1,08-2,67];  $p = 0,02$ ) ont été associés de manière indépendante à la non prescription des AVK. Les facteurs cités par l'urgentiste comme associés à la non prescription des AVK étaient liés: aux caractéristiques du patient ( $n=38,34\%$ ), au médecin urgentiste ( $n=62,55\%$ ), à l'environnement du patient ( $n=20,17\%$ ) et au médicament ( $n=22,23\%$ ).

**Conclusions :** La prescription des AVK était faible. Les raisons de non prescription des AVK étaient liées à plusieurs facteurs inhérents au patient et au degré d'adhésion du médecin aux recommandations.

### M o t s - c l é s

Fibrillation auriculaire - Service des urgences médicales – Anticoagulation.

### S U M M A R Y

**Introduction:** The vitamin K antagonists (VKAs) are currently the most effective therapeutic class for the prevention of cerebrovascular events in atrial fibrillation (AF) patients. However, several studies showed an under-prescription of this therapy.

The aim of the study was to assess the prescription of VKAs in non-valvular AF (NVAF) patients and factors influencing the non-prescription of such treatment.

**Methods:** We conducted a prospective, observational study in an emergency department (ED). Patients with high thromboembolic risk NVAF and not receiving VKAs beforehand were included. Calculation of CHA2DS2-VASc and HAS-BLED scores was performed. An analytic study was conducted in order to identify independent predictors of the under-prescription of VKAs.

**Results:** During study, 176 patients were enrolled, the mean age was  $67 \pm 13$  years and 66% were women. The mean CHA2DS2VASc and HASBLED scores were  $2.88 \pm 1.55$  and  $1.52 \pm 1.05$ , respectively. Among our cohort, VKA was prescribed in 36% of cases. Age  $> 70$  years (OR=1.59, 95%CI [1.11-2.21],  $p < 0.001$ ), creatinine level  $\geq 110 \mu\text{mol/l}$  (OR=2.54, 95%CI [1.20-5.37],  $p = 0.01$ ) and aspirin use (OR =1.7, 95%CI [1.08-2.67],  $p = 0.02$ ) were independently associated with under-prescription of VKAs. Bedside, the main causes reported by the emergency physicians (EP) were: factors related to patient characteristics ( $n=38,34\%$ ), factors related to emergency physician ( $n=62,55\%$ ), factors related to the patient environment ( $n=20,17\%$ ) and factors related to the drug ( $n=22,23\%$ ).

**Conclusions:** Our results showed that the prescription of VKAs was low in ED. The reasons of VKA under-prescription are linked usually to several factors inherent to patient and to the adherence of EP to new recommendations.

### Key - words

Non valvular atrial fibrillation - Anticoagulation - Underuse - Emergency Departments.

Atrial fibrillation (AF) is the most common significant cardiac rhythm disorder encountered in emergency departments (EDs) being present in 3.6 to 7% of general emergency visits (1, 2). It affects 2 to 5% of the general population, and increases substantially with age (3-5). Patients with AF have at least a 5-fold increased risk of ischemic stroke (6). Stroke prevention is therefore crucial to reduce mortality and disability in patients with AF, and especially in those with the highest risk of embolic events (7). Major randomized primary prevention trials conducted in patients with AF have shown that oral anticoagulation (OAC), reduce the risk of embolic events (7-11).

The vitamin K antagonist (VKA) is currently the most prescribed therapeutic class for the prevention of embolic events. However, hemorrhagic stroke is the major complication of VKA, it come to the forefront of iatrogenic accidents and are responsible for approximately 1.1 to 7.4% per year (12,13).

It is therefore essential to accurately assess the benefit / risk ratio of VKA to each patient to whom anticoagulation is proposed. Diverse studies conducted in the hospital setting, in general practice, and in EDs have found that anticoagulation is prescribed to less than 55% of eligible patients (14). Several reasons of this underuse have been reported in the literature.

For some, it is the need for frequent blood tests (15,16), for others, it is factors related to patient itself such as advanced age ( $\geq 80$  years), alone or in combination of another hemorrhagic risk factor (17).

EDs play a substantial role in AF management, notably, concerning stroke prophylaxis. On the other hand, a significant proportion of AF patients attending EDs are at high risk of stroke and are not receiving anticoagulants (18). Therefore, these patients may benefit from adequate prescription to improve their prognosis and long-term quality of life. In this perspective, we conducted this study whose objectives were to assess the prescription of VKAs in non-valvular AF (NVAf) patients and factors influencing the non-prescription of this therapy.

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## METHODS

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We conducted a prospective, observational and mono-centric study in an ED over a period of two years (April 2013 to April 2015).

### Patient selection:

We included consecutive patients older than 18 years, attended to the medical area of the ED during the study period, with the diagnosis of AF eligible for anticoagulation by VKA according to guidelines of the European Society of Cardiology (ESC) (3).

AF was documented in an electrocardiogram (ECG) obtained when the treating physician considered it necessary during clinical evaluation.

Exclusion criteria for the study were valvular AF, patients

receiving OAC, low risk of stroke ( $\text{CHA}_2\text{DS}_2\text{-VASc}=0$ ), contraindications to VKA and hemodynamic instability.

### Data collection:

Data collected from patients included demographic data, comorbidities, disability, type of AF (first episode, paroxysmal, persistent and permanent), risk factors for stroke according to the  $\text{CHA}_2\text{DS}_2\text{-VASc}$  scores, bleeding risk–prediction factors according to the HAS-BLED score, symptoms that caused ED consultation, clinical presentation and ED evaluation, arrhythmia management (rhythm or rate control), patients' outcome (symptom relieving and type of cardiac rhythm at discharge) , final disposition (discharge, admission, or death) and stroke prophylaxis prescribed in the ED (anticoagulation, antiplatelet therapy, or both).

Patients with a  $\text{CHA}_2\text{DS}_2\text{-VASc}$  score  $\geq 1$  are classified as at high risk of stroke, and therefore anticoagulation is recommended in patients without contraindications. VKA was prescribed in a dose-adjusted approach to achieve an international normalized ratio (INR) target of 2.5 (2-3). If anticoagulation was not prescribed, a discussion has been written by the emergency physician explaining the reasons why did not give VKA with detailed arguments on the benefit/ risk of OAC before discharge of the patient.

Patients were divided into two groups: VKA+ Group: patients received VKA and VKA – Group. The two groups were analyzed and compared in order to identify factors independently associated with VKA under-prescription.

### Data Analysis:

Statistical analysis was carried out with SPSS (version 18.0) statistical software package. Continuous variables are presented as means  $\pm$  standard deviation (SD) and discrete variables as absolute values and percentages.

An univariate analysis comparing the two groups was performed, with the chi-square test with Yates' correction or Fisher's exact test when appropriate, odds ratio (OR) with 95% confidence intervals (CI), and the unpaired *t*-test.

The logistic regression analysis with no prescription OAC as dependent variable was there run. The analysis was performed with a binary logistic regression and "enter" method, with an entry criterion of 0.05 and a removal criteria of 0.10. Differences were considered to be statistically significant with  $P < .05$  or when the 95% confidence interval (CI) of the odds ratio (OR) excluded the value of 1.

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## RESULTS

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### Characteristics of the study population

Between April 2013 and April 2015, 126,800 patients were presented to the ED, 249 of these patients were found to have AF and 176 patients were included in the study (Figure 1).

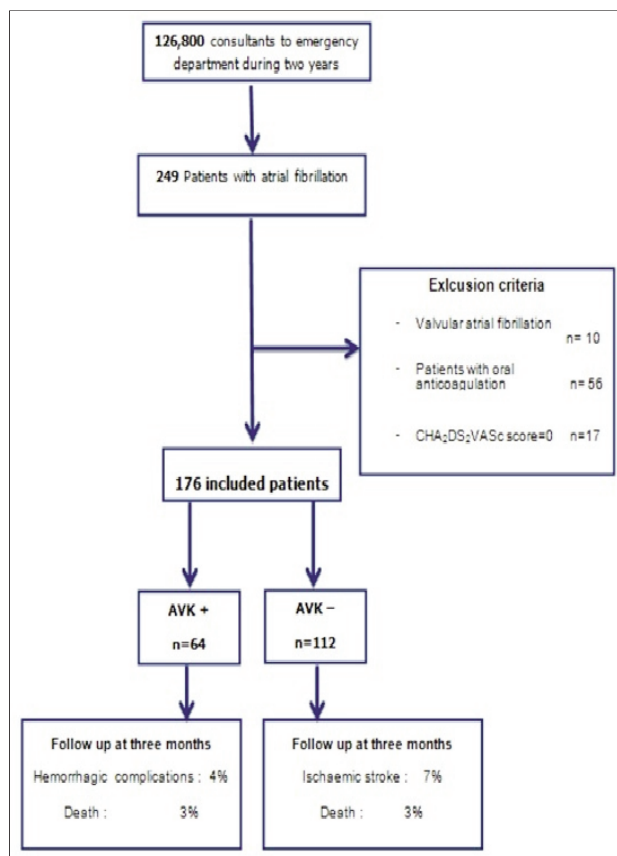


Figure 1 : Algorithm of included patients and outcome

Mean age of these patients was  $67 \pm 13$  years and 117 (66%) of them were women. In 26.7% of the cases, AF was permanent, and in 75% of the patients AF was diagnosed de novo during the ED study visit. Main comorbidities were hypertension (62%), structural heart disease (30%) and diabetes (27%). The mean CHA<sub>2</sub>DS<sub>2</sub>-VASc score was  $2.88 \pm 1.55$ . The mean HAS-BLED score was  $1.52 \pm 1.05$ . A high bleeding risk (HASBLED score  $\geq 3$ ) was found in 18% of patients. Only sixty-four patients (36%) were received VKA at ED. Anticoagulation prescription according to the CHA<sub>2</sub>DS<sub>2</sub>-VASc score was illustrated in figure 2. Rhythm control (in patients with AF duration  $\leq 48$  h) was performed in 17% of patients and rate control (in patients with AF  $>48$  h) in 40% of patients. Eighty-eight percent (88%) of patients were discharged home from ED.

#### Factors associated with the non-prescription of VKA:

The table 1 shows demographic and clinical characteristics of the two groups (VKA+ vs. VKA-). Factors independently associated with lack of oral anticoagulation prescription in eligible patients on logistic regression analysis were listed in table 2.

#### Reasons provided by physicians to explain why patients were not receiving VKA:

For each patient not receiving VKA, the EP in charge of prescribing noted the different criteria justifying the therapeutic abstention. The most frequently found criteria were showed in table 3.

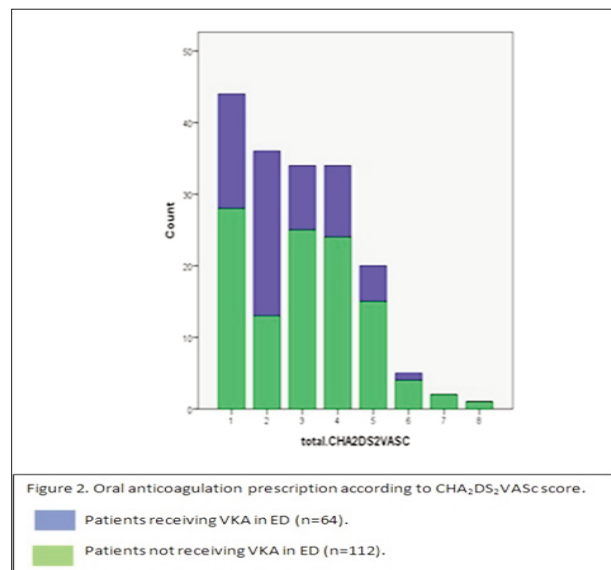
Figure 2 : Oral anticoagulation prescription according to CHA<sub>2</sub>DS<sub>2</sub>-VASc score

Table 1 : Demographic and clinical characteristics of the two groups

Characteristics	Group VKA+ (n=64) 36%	Group VKA- (n=112) 64%	P
<b>Demographics</b>			
Age, mean (SD), years	61±12	69±13	<0.001
Age≥75 years n(%)	9 (14)	47 (42)	<0.001
Male gender n(%)	17(26)	42(37)	0.13
Sex ratio	0.36	0.6	0.11
<b>Risk factors (%)</b>			
Hypertension	38 (64)	72 (64)	0.5
Congestive heart failure	7 (11)	27 (24)	0.02
Coronary disease	3 (5)	16 (14)	0.07
Diabetes	19 (30)	28 (25)	0.5
Dyslipidemia	9 (14)	11 (10)	0.4
Previous AF	8 (12)	35 (31)	0.004
Previous stroke	3 (4)	7 (6)	0.7
COPD	11 (17)	13 (11)	0.3
Dysthyroidism	1 (1)	4 (3)	0.6
Renal failure	1 (1)	4 (3)	0.5
<b>Type of AF (%)</b>			
Paroxysmal (<48 hours)	30 (47)	38 (34)	0.09
Paroxysmal (>48 hours)	21 (33)	25 (22)	0.13
Persistent	5 (8)	10 (9)	0.8
Permanent	8 (12)	39 (35)	0.06
More than 3 drugs per day	13 (20)	42 (37)	0.01

COPD: Chronic obstructive pulmonary disease

**Table 2** : Factors independently associated with lack of oral anticoagulation prescription

	Adjusted OR	CI 95%	P
Age $\geq 70$ years	1.59	[1.11-2.21]	<0.001
Creatinine level $\geq 110\mu\text{mol/L}$	2.54	[1.20-5.37]	0.01
Aspirin use	1.7	[1.08-2.67]	0.02

**Table 3** : Reasons given by physicians to explain why patients were not receiving oral anticoagulation

Reasons given by physicians to explain why patients were not receiving VKA	n	%
<b>Factors related to patient characteristics :</b>	38	34
. cognitive impairment	12	32
. physical dependence	26	68
<b>Factors related to EP:</b>	62	55
. concept of "clinical inertia" (old age)	24	38
. fear of side effects interesting the fear of bleeding	16	26
. ignorance of recommendations	22	36
<b>Factors related to patient environment:</b>	20	17
(social isolation and poor socioeconomic conditions)		
<b>Factors related to drugs:</b>	22	23
(polymedication and adherence to treatment)		

## DISCUSSION

Our study has shown that the prescription rate of VKAs was low (36%). Factors independently associated with the prescription were related to the characteristics of the patients (advanced age, using aspirin and past medical history of renal failure). The leading reason why patients were not receiving OAC was a «potential contra-indication» (especially advanced age), followed by «lack of knowledge of recommendations», cognitive impairment and physical dependence of patient and «fear of bleeding». The medical management of AF (other than antiarrhythmic drugs) is primarily focused on reducing the risk of stroke. The prevention of thromboembolic events is based on the establishment and monitoring of anticoagulation now mainly based on the use of VKA. This preventive treatment is a well codified theory, based on the thromboembolic risk assessed by the CHA<sub>2</sub>DS<sub>2</sub>-Vasc score (3).

Although the VKA prescription rates increased over time since the publication of AFASAK, BAATAF, SPAF, CAFA, SPINAF studies between 1989 and 1992, an under-prescription of VKA has been observed in patients with NVAf at high thromboembolic risk (9-11,19).

VKA prescription rates in patients with AF vary from 28-64%. In elderly patients (from 75 to 80 years), it vary from 35 to 46% (20,21).

We found that despite a mean age of patients more than 65 years, with high risk of thromboembolism, the

prescription of VKA was around 36%. These data were consistent with the results of many recent studies (22-24). Patients not receiving VKA were older (69 vs. 61 years,  $p<0.001$ ), had higher prescription medication including more than 3 drugs per day (37 vs. 20%,  $p=0.01$ ) and higher HASBLED score ( $3.09 \pm 1.64$  vs.  $1.17 \pm 0.8$ ,  $p<0.001$ ). The number of ischemic stroke was higher in the VKA- group, and bleeding events were more frequent in the VKA + group. The mortality rate was similar in both groups.

Advanced age ( $>70$  years) was independently associated with the lack of anticoagulant prescription to eligible patients. These data are consistent with those in other studies in which the elderly population was often excluded from anticoagulant treatment (18, 25-30). The fear of bleeding is one of the main barriers in these patients, and may override the perception of these patients' risk of stroke (31-33).

It was provided as one of main explanations by our physicians. They probably consider that it is more serious to have severe bleeding because of properly prescribed and managed OAC, than to have severe embolic events in the absence of OAC. These explanations had already been suggested (3,31,33). But different studies have demonstrated that anticoagulation in this population reduces the risk of stroke without a significant increase of bleeding and that the net benefit of anticoagulation is greater than in younger patients (34-38).

One of the major reasons provided in SAFE II by GPs, and sometimes cardiologists, not to prescribe OAC, was that they thought there was no indication (31,32). This reason was provided by 36% of physicians in our study.

This finding supports the hypothesis that the main reason why NVAf patients are not receiving OAC in practice is a lack of knowledge of trials and guidelines.

Because the guidelines' recommendations have been demonstrated to be widely applicable in daily practice (3,30,35), and previous studies in local settings have demonstrated the usefulness of specific training to improve management's adequacy, educational efforts to increase physicians' adherence to the guidelines appear warranted (39).

Previous cognitive impairment, falls or gait disturbances and living conditions were often considered as major contra-indications for OAC. These factors have not been clearly evaluated until now and should be only considered on an individual basis when the risk of such a condition appears higher than that of the natural history of the disease.

Because stroke is the major risk of AF and because OAC can drastically reduce this risk, primary and secondary prevention of ischaemic stroke among patients with AF by an appropriate use of OAC is a crucial issue to improve quality of care.

## STUDY LIMITATIONS

The main limitation of this study is the small number of patients; this does not reflect the real rate of the VKA prescription in the other ED and cardiology department. Another limitation is that our data lack objective assessment of cognitive status, falls or gait disturbances and living conditions.

## CONCLUSION

In This study, the prescription of VKA in patients with high thromboembolic risk NVAF was low in ED. The reasons of VKA under-prescription are linked usually to several

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