DeepRaft

Doctors' Education, Empowerment of Patients, Regarding Atrial Fibrillation & venous Thromboembolism

D1.1 AF/VTE Current Practices and public views report

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Improving the Identification and Management of Patients with Atrial Fibrillation (AF) in Order to Reduce Stroke Risk and Venous Thromboembolism (VTE) in Eastern Europe

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AF/VTE Current Practices and public views report

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is a leading cause of mortality and morbidity. The prevalence of AF in the adult population is nearly 3% and increases with age (1). The main negative impact of AF is the 5-fold increased risk of stroke (2). Furthermore, AF is also associated with increased morbidity due to development of heart failure (3). From the patient and the health system perspective, AF causes impaired quality of life and increases health care costs. Finally, AF is independently associated with a two-fold increased risk of all-cause mortality in women and a 1.5-fold increase in men (4).

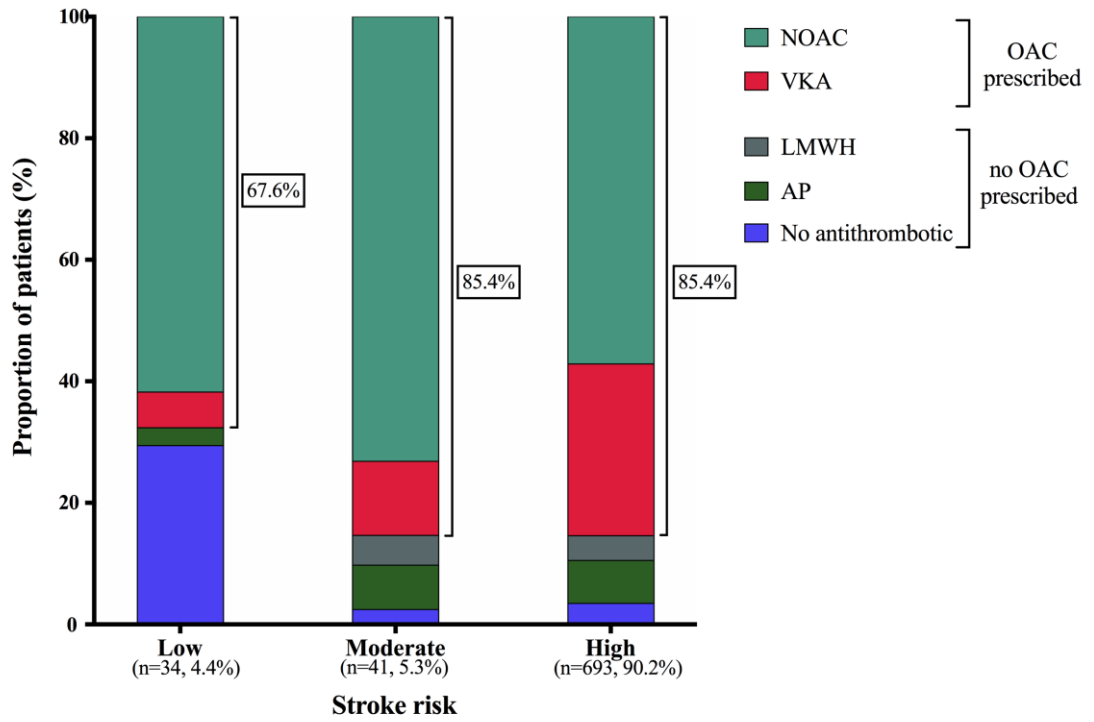
In total, 20–30% of patients with an ischaemic stroke have AF diagnosed before, during or after the initial event (5). At least two thirds of strokes due to AF can be prevented with the use of anticoagulation. Lately, after the introduction of non-vitamin K antagonist oral anticoagulants (NOACs), results from meta-analyses and healthcare databases have shown that NOACs are safer and slightly more effective compared to vitamin K antagonists.

An accurate diagnosis of AF is very important to the general health of an individual patient; nevertheless, this is complicated by the fact that AF may be a paroxysmal episode of arrhythmia, and therefore it may be missed without continuous rhythm monitoring. A substantial proportion of individuals with AF may be asymptomatic and thus, AF may not be detected until after a cerebrovascular event (6). However, most strategies for early identification of AF are difficult to be implemented from healthcare providers and patients. For instance, although it is recommended by international guidelines that targeted/opportunistic screening of symptomatic patients or those with risk factors may allow identification of AF patients, this has not been properly disseminated in providers of AF-related services. In data from a cluster randomised trial of opportunistic versus targeted screening in general practices, 172 patients would have to be screened systematically and 167 would have to be screened opportunistically to detect one additional case of atrial fibrillation (7).

Gap analysis in anticoagulation practices from the largest AF database in Greece

We recently published data from our academic center in AHEPA University Hospital in Aristotle University of Thessaloniki, Greece on real-world anticoagulation strategies of patients hospitalized with AF. We report that one out of six AF patients newly discharged from the hospital may be treated discordantly to the corresponding risk for stroke (8). Specifically, 15 percent were not receiving OAC despite significant stroke risk, whereas seven percent were receiving OAC despite insignificant stroke risk. Patients at moderate stroke risk were largely covered with OAC (see Figure 1):

Figure 1. Stratification of antithrombotic discharge regimens according to stroke risk



OAC-treated groups are marked with brackets.
AP, antiplatelet; LMWH, low molecular weight heparin; NOAC, non-vitamin K antagonist oral anticoagulant; OAC, oral anticoagulant; VKA, vitamin K antagonist.

High-risk patients are sometimes discharged without OAC therapy! This 'risk-treatment paradox', as pointed out by Cullen et al.,(9) may be more prominent in acutely hospitalized patients, also resembling our study population. It may be speculated that the severity of these patients' primary illnesses draws the clinicians' attention away from provisioning OAC treatment. Others have shown that undertreatment of high-stroke-risk AF varies from 20% to more than 50% in different settings (10–14). In a worldwide study by Huisman et al., 16.8% of patients with a CHA_2DS_2-Vasc score ≥2 received no OAC (15).

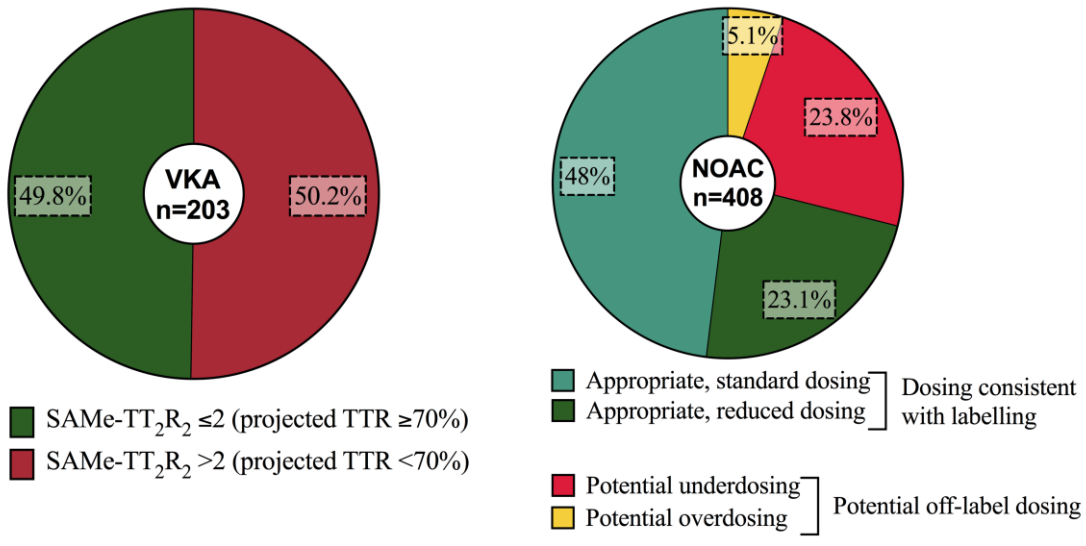
Oral anticoagulation prescribing in most of our patients with zero nongender-related stroke risk factors could have occurred for transient purposes, such as postcardioversion or post-AF ablation. Indeed, guidelines suggest a short-term anticoagulation in all patients

at low stroke risk after cardioversion of AF of >48 hours duration (16). A large multicenter registry has also reported a high rate (approximately 50%) of OAC use in low stroke risk AF, although it was focused on stable outpatients (9).

We also performed a quality analysis of specific prescribed OAC regimens, namely VKAs and NOACs (Figure 2). We found as much as half of VKA prescriptions expected to underperform in terms of stroke prevention, as evaluated by the SAMe-TT_2R_2 score (Sex, Age, Medical history, Treatment, Tobacco use, Race). The latter is a score able to a priori gauge the probability of an applied VKA regimen to achieve a satisfactory time in therapeutic range (TTR) (17). Hospitalization is an excellent opportunity to evaluate VKA users or OAC candidates in general and opt for NOAC initiation (or switch) if their SAMe-TT_2R_2 score corresponds to a TTR <70%.

More than a quarter of administered NOAC regimens did not comply with the labelled recommendations regarding stroke prevention. 'Potential off-label dosing', included 'potential underdosing' (i.e., indication for standard dose, received reduced dose) and 'potential overdosing' (i.e., indication for reduced dose, received standard dose). In-hospital physicians' role is complex when opting for a dose at discharge; they must weigh evolving patient clinical profiles, such as dynamic changes in renal function, newly diagnosed comorbidities and new interacting medication, as well as competing thrombotic and hemorrhagic risk. Thus, they may deliberately overdose or underdose a patient, e.g., when observing a trend in renal function during hospitalization.

Figure 2. Assessment of VKA and NOAC discharge regimens, according to the SAMe-TT_2R_2 score and European NOAC-specific labelling respectively.



NOAC, non-vitamin K antagonist oral anticoagulant; TTR, time in therapeutic range; VKA, vitamin K antagonist.

Several factors were associated with suboptimal anticoagulation practices in our registry. Paroxysmal AF, a major bleeding episode and concomitant antiplatelet therapy were associated with non-prescribing of OAC to high-risk patients. When dosing NOACs,

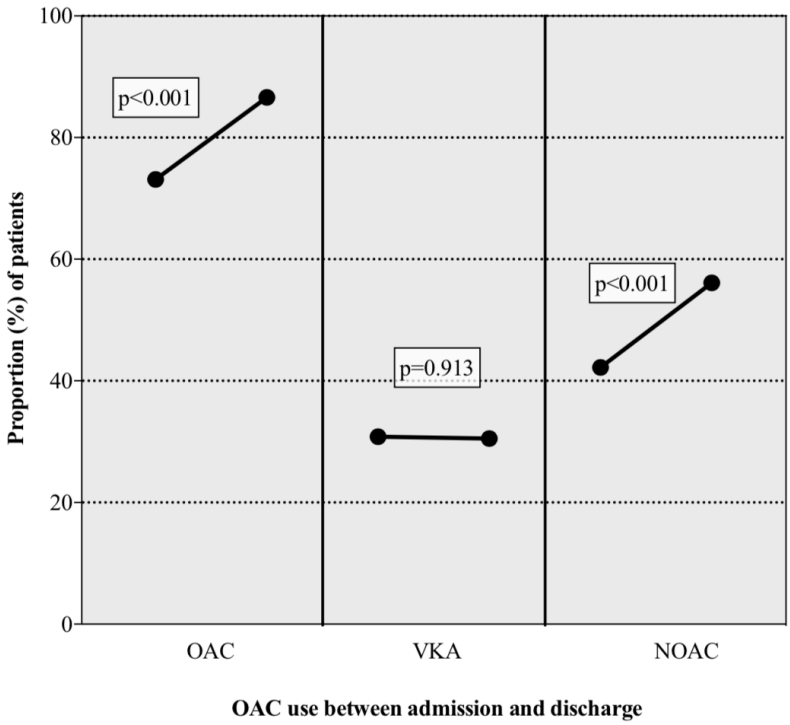
physicians may overestimate the potential bleeding risk, compared to the benefits of stroke reduction, even more in the face of a previous cerebrovascular event.

Nevertheless, most health registries cannot explain suboptimal OAC use by plain epidemiological correlations. From the patient perspective, these relate to education, support and monitoring on the one hand, and ensuring appropriate and effective stroke prophylaxis on the other hand. Arguably, these tasks should not require resource intensive interventions or ancillary health care staff to be achieved. Instead, a new paradigm is imperative to empower both physicians and patients to realize these ends, and we submit that this becomes an unmet need in view of the rapid growth in the AF population.

Another cross-sectional study stemming from the same database was recently published from our academic center. This time the focus was on pre- and post-hospitalization OAC regimens of patients with known AF at high-stroke risk. Key findings were as follows:

a) hospitalization was associated with an increase in OAC use by 13.5%, attributed mainly to a similar increase in NOAC use (Figure 3):

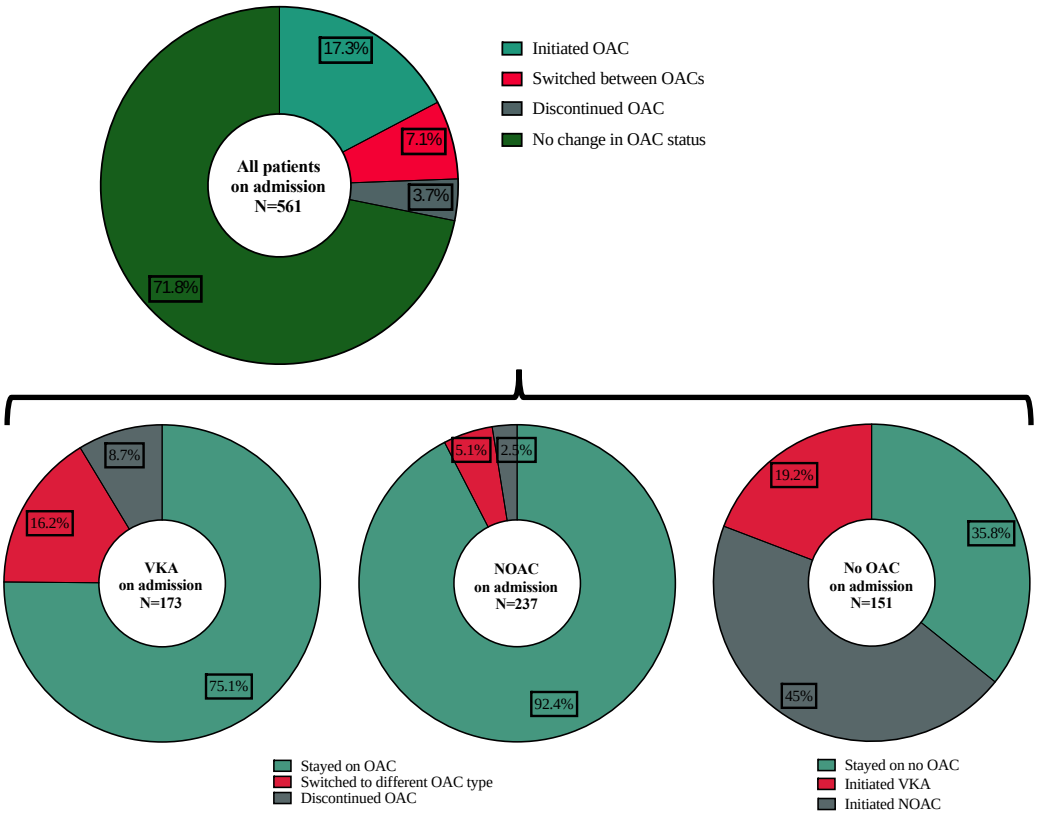
Figure 3. Assessment of pre- and post-hospitalization trends in anticoagulation treatment



Significance of changes regarding each OAC type is assessed with McNemar's test
NOAC, non-Vitamin K Oral Anticoagulant; OAC, oral anticoagulant; VKA, vitamin K antagonist.

b) treatment changes between pre- and post- hospitalization OAC regimens were identified in 3 out of 10 patients. Most of these patients were started OAC at discharge, predominantly NOAC. Switching or discontinuing OAC at discharge was three times more common among prior VKA users compared to prior NOAC users (Figure 4):

Figure 4. Assessment of changing rates in oral anticoagulation treatment triggered by hospitalization



AF, atrial fibrillation; NOAC, non-Vitamin K Oral Anticoagulant; OAC, oral anticoagulant; VKA, vitamin K antagonist

Information regarding best versus real-world practice in AF, along with identified gaps is summarized below:

Atrial fibrillation		
Best Practice	**Gap**	**Current Practice**
Early detection of AF may reduce the risk of stroke by early initiation of treatment	Physicians need to improve screening rate for early detection of AF	20–30% of patients with an ischaemic stroke have AF diagnosed before, during or after the initial event
Patients with AF may present early with atypical symptoms or very late with heart failure or a stroke	Physicians need to increase their clinical suspicion of AF based on patient symptoms. Moreover, patients need to increase their awareness on AF and its negative outcomes in their personal well-being	At least a third of AF patients, mainly the elderly ones, do not report typical AF symptoms or report being asymptomatic
Proper OAC use reduces stroke rates by at least two-thirds	Physicians need to apply OAC according to stroke risk	One out of six AF patients newly discharged from the hospital may be treated discordantly to the corresponding risk for stroke. OAC coverage rises following a hospitalization
	Physicians could evaluate patient profile and opt for NOAC initiation (or switch) if the SAMe-TT2R2 score corresponds to a TTR <70%	Half of VKA prescriptions are expected to underperform in terms of stroke prevention. Patients who switch OAC type at discharge are predominantly prescribed NOACs
	Physicians need to apply NOACs according to each drug's SPS. Each NOAC should be dosed according to several patient profile parameters (age, kidney function, weight, concomitant medication)	More than a quarter of NOAC regimens do not adhere to labeled recommendations regarding stroke prevention
NOAC use is contraindicated in valvular AF	Physicians should exclude patients with mechanical valves or moderate to severe mitral valve stenosis of rheumatic aetiology from NOAC use	OAC medication is often prescribed without elaboration on prior cardiac operations or rheumatic mitral valve disease

Patient compliance to OAC treatment is crucial for optimal outcomes	Physicians may regularly assess patient compliance to OAC treatment with use of specific surveys or questionnaires (EHRA web-site, Morisky questionnaire)	More than quarter of patients do not adequately adhere to their prescribed OAC treatment
Interaction of NOACs with concomitant medications can increase bleeding risk and decrease efficiency	Physicians need to assess possible interaction effects of concomitant medications and adjust NOACs dose	At least a third of AF patients do not report all concomitant medications to their doctors
High awareness of AF patients about risks, complications, prognosis and treatment tactics	It's not always possible for doctors to clearly inform patients about risks, complications, prognosis and treatment tactics (time limit, communicative skills, patient's education level)	Only around 20% of AF patients recognize possible risks associated with their disease and can access information on modern principles of AF treatment
Early diagnosis of AF increases patient's chances for optimal management of the arrhythmia	The doctors could include opportunistic screening for AF when examining patients at risk. Short-term ECG or pulse palpation (followed by ECG in case of an irregular pulse) has been proven cost-effective in elderly populations (>65 years)	The assessments during a physical exam often rely on automated machines (e.g. blood pressure device) that may fail to point out an irregular rhythm. The diagnosis of AF may be elusive, since at least a quarter of patients do not report specific symptoms of their arrhythmia

Venous thromboembolism

The most common presentations of venous thromboembolism (VTE) are deep vein thrombosis (DVT) of the lower extremity and pulmonary embolism (PE). Acute pulmonary embolism (PE) is the most striking clinical manifestation of venous thromboembolism (VTE) and the third most frequent acute cardiovascular disease.

The estimated annual PE-related mortality in Europe exceeds 500,000 deaths (18). Between 5% and 15% of patients suffering acute PE die within 30 days, and of those who survive, as many as 30% develop potentially life-threatening recurrence or some kind of chronic disabling problems. In addition, a number of PE patients ranging between 1% and 4% will develop a severe complication named chronic thromboembolic pulmonary hypertension (19). Taken together, these numbers emphasize the impact of acute VTE and PE on acute and long-term morbidity and mortality, as well as on the quality of life of the affected patients. Besides, they highlight the substantial PE-related economic burden for national health systems. In fact, it was recently calculated that direct and indirect costs associated with VTE in the European Union Member States amount to € 13.2 billion per year, with potential cost savings of up to € 7.2 billion if prevention and management of the disease could be optimized

Anticoagulation is the mainstay of therapy for VTE, as it is for AF. Long-term anticoagulant therapy is administered beyond the initial few days of anticoagulation for a finite period of typically three to six months. Options for long-term anticoagulation include OACs (both VKAs and NOACs) and parenteral subcutaneous anticoagulants. While the factor Xa and thrombin inhibitors are typically preferred, choosing among these options frequently depends upon clinician experience and availability, the risks of bleeding, patient comorbidities and preferences, cost, and convenience (20).

Patient values and preferences are critical in selecting a long-term agent for anticoagulation in acute venous thromboembolism (VTE). Variations exist in the perceptions of burden by patients. For example, while some patients want to avoid daily injections, others may consider them preferable to weekly international normalized ratio (INR) monitoring. As another example, patients who place a high value on cost may choose VKA, while others who place a high value on a lower risk of bleeding may prefer the direct oral anticoagulants (21).

All patients with established VTE should undergo a thorough history and physical examination combined with review of diagnostic imaging studies and routine laboratory testing (22). This may reveal an acquired condition (eg, major surgery) predisposing to the thrombotic event or provide clues to the presence of inherited thrombophilia (eg, first-degree relatives with VTE at a young age). As venous thrombosis is a multifactorial disorder, some patients will have more than one major risk factor.

Today, after a long period of relative inactivity, prevention and management of VTE is increasingly becoming top priority issues worldwide thanks, (i) to an increased awareness of their medical and social burden; and (ii) to the substantial recent advances in diagnostic and treatment options. However, a number of unresolved issues exist such as:

- the reduced clinical suspicion threshold, resulting in a lower proportion of VTE among suspected patients;
- the challenge of diagnosing VTE in special patient populations, such as elderly patients, pregnant women, or patients with a prior VTE.
- the challenge of diagnosing VTE in regards to subsegmental pulmonary embolism
- the overdiagnosis and overtreatment of VTE, especially regarding calf deep-vein thrombosis and subsegmental pulmonary embolism
- the optimal antithrombotic agent in high-risk patients
- the optimal timing of thromboprophylaxis initiation in special populations such as the surgical population, patients with severe comorbid conditions, pregnant women.
- the duration of prophylaxis for the prevention of initial and recurrent VTE events
- the long-term treatment after an episode of unprovoked episode of VTE
- the low commitment of patients to the prolonged anticoagulant therapy the low commitment of patients to regular INR control

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