European Heart Journal (2006) **27**, 3018–3026
doi:10.1093/eurheartj/ehl015

Antithrombotic treatment in real-life atrial fibrillation patients: a report from the Euro Heart Survey on Atrial Fibrillation

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Received 9 January 2006; revised 7 April 2006; accepted 13 April 2006; online publish-ahead-of-print 26 May 2006

KEYWORDS
Atrial fibrillation;
Stroke;
Antithrombotic therapy;
Oral anticoagulation;
Guidelines;
Risk stratification

Aims To describe guideline adherence and application of different stroke risk stratification schemes regarding antithrombotic therapy in real-life atrial fibrillation (AF) patients and to assess which factors influence antithrombotic management decisions.
Methods and results The Euro Heart Survey enrolled 5333 AF patients in 35 countries, in 2003 and 2004. Prescription of antithrombotic drugs, especially oral anticoagulation (OAC), was hardly tailored to the patient's stroke risk profile as indicated by the joint guidelines of the American College of Cardiology, American Heart Association, and the European Society of Cardiology, ACCP guidelines, or $CHADS_2$ and Framingham risk scores. In multivariable analysis, only a limited number of the well-known stroke risk factors triggered OAC prescription. In contrast, less relevant factors, of which clinical type of AF and availability of an OAC monitoring outpatient clinic were the most marked, played a significant role in OAC prescription. Electrical cardioversions and catheter ablations clearly triggered OAC prescription, whereas pharmacological cardioversions even in the presence of stroke risk factors did not.
Conclusion Antithrombotic therapy in AF is hardly tailored to the patient's stroke risk profile. Factors other than well-known stroke risk factors were significantly involved in antithrombotic management decisions. To facilitate this tailored treatment, guideline writers and physician educators should focus on providing one uniform and easy to use stroke risk stratification scheme.

Introduction

Atrial fibrillation (AF) is a risk factor for stroke and thrombo-embolism.[1] When stroke occurs in association with AF, there is a higher mortality and greater disability.[2] Stroke prevention is therefore a major issue when managing patients with AF, and many clinical risk factors have been identified, which confer a high risk of stroke, and oral anticoagulation (OAC) is recommended for such patients.[3,4] In the Euro Heart Survey, 90% of AF patients had at least one or more additional risk factors for stroke.[5] These risk factors have been used to inform the development of various risk stratification criteria, which are used to aid decision-making for thromboprophylaxis.[3,4,6,7]

Many observational studies have shown that OAC is frequently underused in AF patients in daily practice, with reported percentages of OAC prescription between 30 and 60%.[8–12] This suboptimal use may, among several reasons, relate to unawareness among clinicians to guidelines and various risk stratification criteria or poor appreciation of the risk–benefit ratio, with overestimation of bleeding risks.[13,14] Although some information is available regarding factors limiting optimal OAC prescription, limited information is available regarding the application of stroke risk stratification schemes, in general as well as around interventions for AF, in real-life clinical practice. Also, it is not well known to what extent stroke risk factors determine the choice for either OAC, antiplatelet drugs, or no antithrombotic therapy.

The first report on the Euro Heart Survey on AF suggested that OAC eligibility hardly determines the prescription of OAC and that other factors might play a role.[5] The present

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analysis provides a detailed description of the application of antithrombotic drugs related to stroke risk stratification schemes in real-life cardiology practice throughout Europe and of the factors that influence the decision-making process. In addition, a description of antithrombotic therapy around pharmacological cardioversion (PCV), electrical cardioversion (ECV), and catheter ablation is given.

Methods

The details of the Euro Heart Survey on AF have previously been described.[5] Patients were enrolled in 182 university, non-university, and specialized hospitals among 35 member countries of the European Society of Cardiology (ESC). Consecutive patients per department were requested from the outpatient cardiology clinic, cardiology ward, first (heart) aid, cardiac surgery ward, cardioversion department, and/or device implantation department. Patients of $\geq$18 years, with AF on ECG or Holter recording during the qualifying admission/consultation or in the preceding 12 months, were enrolled. Enrolment took place in 2003–04. Data were collected from medical records and/or medical information systems, and patient management was according to usual local practice. Central data collection was done at the European Heart House of the ESC, Sophia Antipolis, France. Data definitions of several important variables as used in this manuscript were also previously reported.[5]

Stroke risk stratification schemes

Antithrombotic drug prescription was analysed with reference to the joint guidelines on AF management of the American College of Cardiology (ACC), the American Heart Association (AHA), and ESC,[3] and also the guidelines on antithrombotic therapy in AF of the American College of Chest Physicians (ACCP).[15] The 2001 ACCP guidelines were recently superseded by the 2004 guidelines,[16] but we focus only on the 2001 guidelines because these were published at the time of the survey. Recommendations for antithrombotic therapy in the latter guidelines do not take into account the patients with first detected AF. In addition, two other stroke risk stratification schemes were used for description of antithrombotic drug use. The $CHADS_2$ (Congestive heart failure, Hypertension, Age $>$75 years, Diabetes mellitus, and Stroke/TIA) stroke risk score is based on stroke risk classification schemes of the Stroke Prevention in Atrial Fibrillation (SPAF) trial investigators and the AF Investigators (AFI) and was validated in the National Registry of AF cohort on patients not receiving OAC.[6] The $CHADS_2$ scheme produces a score from 0 to 6 for patients with non-valvular AF. The Framingham stroke risk score is a population-based score derived from longitudinal follow-up in the Framingham Heart Study and is applicable to patients with newly detected non-valvular AF and produces a score from 0 to 31[7] (see Appendix for an exact description of all four-stroke risk stratification schemes).

Data analysis

Data analysis was done at the Department of Cardiology, University Hospital Maastricht, Maastricht, The Netherlands. Data analysis was performed with SPSS (SPSS Inc., release 12.01) and Stata (Stata corporation, release SE 8.0) statistical software. In *Tables 1* and *6*, continuous variables are reported as mean ($\pm$standard deviation) and categorical variables as observed number (percentage within the column). In both the tables, numbers can add up to a lower

Table 1 Characteristics vs. antithrombotic drug use of 2706 patients in whom no PCV or ECV or catheter ablation was performed or planned

	OAC only	OAC + antiplatelet	Antiplatelet only	No antithrombotic drug	*P*-value
n	1532	201	739	234	
Admission/visit					
OAC clinic available	1074 (71)	118 (59)	455 (62)	158 (68)	<0.001
Reason for visit					
AF only	440 (29)	37 (19)	163 (22)	102 (44)	<0.001
AF + other reason	723 (47)	114 (57)	365 (50)	72 (31)	
Other reason only	365 (24)	49 (25)	209 (28)	60 (26)	
Demographics					
Age (years)	69 $\pm$ 11	69 $\pm$ 11	71 $\pm$ 12	64 $\pm$ 18	<0.001
Female gender	709 (46)	73 (36)	313 (42)	101 (43)	0.025
Stroke risk factors					
Valvular heart disease	283 (19)	29 (15)	23 (3)	9 (4)	<0.001
Any thrombo-embolism	252 (17)	44 (22)	105 (14)	15 (7)	<0.001
Stroke/TIA	202 (13)	31 (16)	89 (12)	14 (6)	0.010
Heart failure	631 (41)	97 (49)	277 (38)	61 (26)	<0.001
Hypertension	979 (64)	130 (65)	522 (71)	120 (51)	<0.001
CAD	480 (32)	134 (68)	340 (47)	36 (16)	<0.001
Diabetes	325 (21)	49 (24)	130 (18)	26 (11)	0.001
Bleeding risk factors					
Major bleeding	31 (2)	6 (3)	14 (2)	16 (7)	<0.001
Malignancy	102 (7)	14 (7)	35 (5)	21 (9)	0.042
Renal failure	97 (6)	14 (7)	52 (7)	16 (7)	0.197
Type of AF					
First detected	134 (9)	18 (9)	109 (15)	49 (22)	<0.001
Paroxysmal	276 (19)	38 (19)	270 (37)	79 (43)	
Persistent	219 (15)	17 (9)	78 (11)	20 (9)	
Permanent	864 (58)	123 (63)	263 (37)	58 (26)	
Heart rhythm strategy					
Rhythm control	355 (24)	60 (30)	201 (28)	77 (34)	<0.001
Rate control	981 (66)	124 (62)	404 (56)	98 (43)	
No rhythm/rate control	158 (11)	16 (8)	111 (16)	52 (23)	

count than the total number of patients in a column, because of missing values. In *Table 1*, the presence of any difference among the four antithrombotic treatment groups was tested with one-way ANOVA for continuous variables and with χ^2 statistic for categorical variables, whereby variables with more than two categories were tested on differences in the distribution of all categories. Whether there was an association between antithrombotic drug prescription and a worsening stroke risk profile was tested for all four schemes by means of χ^2 for trend. For these analyses, the very small groups of combination therapy and heparin only were left out, in order to assume an ordinal nature of the antithrombotic therapy, i.e. OAC—antiplatelet drug—no drug. Following this analysis, to test whether the (absence of) increasing trend was present for all categories, all adjacent risk categories were pairwise compared by means of χ^2 statistic. All the above-mentioned tests were two-sided.

Prevalence of stroke risk factors and stroke risk categories was reported per stroke risk stratification scheme among patients who survived hospital admission and for whom the concerning scheme was designed. Antithrombotic drug prescription at discharge was reported in the same patients as described above, with the addition that patients in whom a PCV, an ECV, or catheter ablation was performed or planned were excluded from the analyses, as these interventions may trigger specific antithrombotic treatment regardless of risk schemes. Antithrombotic treatment around these interventions was analysed separately.

Multivariable stepwise logistic regression was performed to identify factors associated with prescribing OAC, with an antiplatelet agent rather than no drug, with any antithrombotic drug rather than no drug, and with a combination of OAC and an antiplatelet agent rather than OAC only. The following 15 variables were put in the multivariable models: age, gender, clinical type of AF, hypertension, heart failure, coronary artery disease (CAD), diabetes, (prior) stroke or transient ischaemic attack (TIA), valvular heart disease (mitral stenosis or valve surgery), (prior) malignancy, (prior) major bleeding, renal failure, presence of an outpatient clinic for OAC monitoring, reason for admission or visit, and rate/rhythm control. Variables were removed stepwise from the model when the *P*-value exceeded 0.10. Variables with $P < 0.05$ in the final model were considered to be significant contributors and were kept in the model. Hereafter, these models were validated by means of bootstrapping, which was performed with 100 samples for each reported multivariable logistic regression analysis. Bootstrapping provided information on the effect stability of each factor as a predictor of the outcome variable. Effects that were instable were stepwise left out of the model, which eventually resulted in the final model containing only stable significant effects, and these final models are reported here. For each variable in this model, the net odds ratio (OR) and its 95% confidence interval (CI), backward elimination log-likelihood ratio χ^2 (-2 LL), degrees of freedom (df), and *P*-value are reported. In addition, predictive accuracy of each model is reported as the area under the ROC curve.

Results

In the Euro Heart Survey, 5333 ambulant and hospitalized AF patients were enrolled. *Table 1* shows characteristics per antithrombotic treatment group of 2706 patients (52%) in whom no PCV, ECV, or catheter ablation was performed or planned at the time of the survey. These factors were tested in multivariable logistic regression analyses on association with antithrombotic drug prescription.

Risk factors for stroke

Figure 1 shows the distribution of stroke risk categories as defined according to the joint ACC/AHA/ESC guidelines on AF management, the ACCP guidelines on antithrombotic therapy in AF, the $CHADS_2$ score, and the Framingham score.

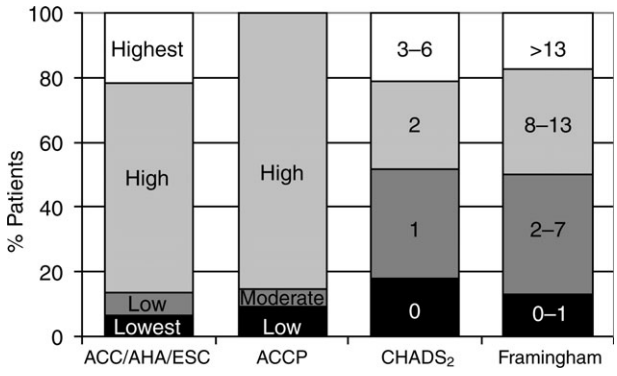

Figure 1 Distribution of stroke risk categories according to the ACC/AHA/ESC and ACCP guidelines and the $CHADS_2$ and Framingham risk scores. For a detailed description of the risk categories, see Appendix.

The low(est) risk category or score was found in 10–18% of patients, and most AF patients in this survey were at (very) high risk for stroke according to both guidelines, whereas higher risk categorization was more shaded according to the $CHADS_2$ and Framingham scores. Hypertension was the main driver for such an impressive prevalence of risk factors, but also heart failure and simply old age were important contributors. For every risk stratification scheme, the exact prevalence of stroke risk factors and classification into risk groups are shown in the Appendix.

Prescription of antithrombotic drugs

Antithrombotic drug prescription significantly ($P < 0.001$) increased with a worsening stroke risk profile according to all four risk stratification schemes (*Figure 2*). However, variation in drug prescription was marginal and a large proportion (40–50%) of patients at the lowest risk were prescribed OAC. Also, when pairwise comparing the adjacent risk categories, some inconsistencies in the increasing trends were found. Prescription in ACC/AHA/ESC high risk was comparable ($P = 0.506$) with the low risk, and prescription in ACCP high risk was comparable with the intermediate risk ($P = 0.753$). Regarding the $CHADS_2$ score, the only pairwise comparison that was significantly different was between score 0 and 1, which was also the case for the Framingham score regarding the comparison of categories 8–13 and >13.

Factors associated with antithrombotic management decisions

Tables 2–5 report factors that were in multivariable logistic regression significantly associated with antithrombotic drug prescription. Of all well-known stroke risk factors, valvular heart disease was strongly associated with OAC prescription, as well as diabetes, although to a much lesser extent. A (prior) stroke/TIA, hypertension, age >75 years and CAD were not associated with OAC prescription, but they were associated with prescription of an antiplatelet drug or any antithrombotic drug. CAD was also a reason to add an antiplatelet drug to OAC. Heart failure did not play a significant role in any of these four analyses. Patients with a (prior) major bleeding were not only less likely to receive OAC, but were also denied antiplatelet drugs.

Several factors other than well-known stroke risk factors played a significant role in these analyses. Patients with persistent or permanent AF were much more likely to receive

OAC than patients with first detected or paroxysmal AF. When AF was the only reason for the admission or visit, OAC was more often prescribed, in comparison, when other medical conditions were in play. The absence of an OAC monitoring outpatient clinic lead to a lower probability of prescribing OAC, and also more frequently to addition of an antiplatelet drug when OAC was prescribed. Patients, in whom no rhythm or rate control drugs or interventions were applied, had a lower chance of receiving OAC.

Antithrombotic drug therapy around interventions for AF

When comparing with patients undergoing cardioversion, patients undergoing catheter ablation were younger, less often female, and had a much lower stroke risk burden (*Table 6*).

Antithrombotic treatment around PCV, ECV, and catheter ablation procedures is depicted in *Figure 3*. Many patients did not receive OAC before and after their PCV, but OAC prescription clearly increased when a PCV was planned. Most patients received antithrombotic treatment around ECV, and OAC prescription was clearly triggered at discharge when an ECV was planned. Among patients who underwent a current PCV, 47% ($n = 924$) received OAC at discharge when at least one stroke risk factor according to the ACC/AHA/ESC guidelines was present, 63% ($n = 50$) when no risk factor was present but AF duration was longer than 48 h or unknown, 48% ($n = 974$) when either at least one risk factor was present or AF duration was longer than 48 h

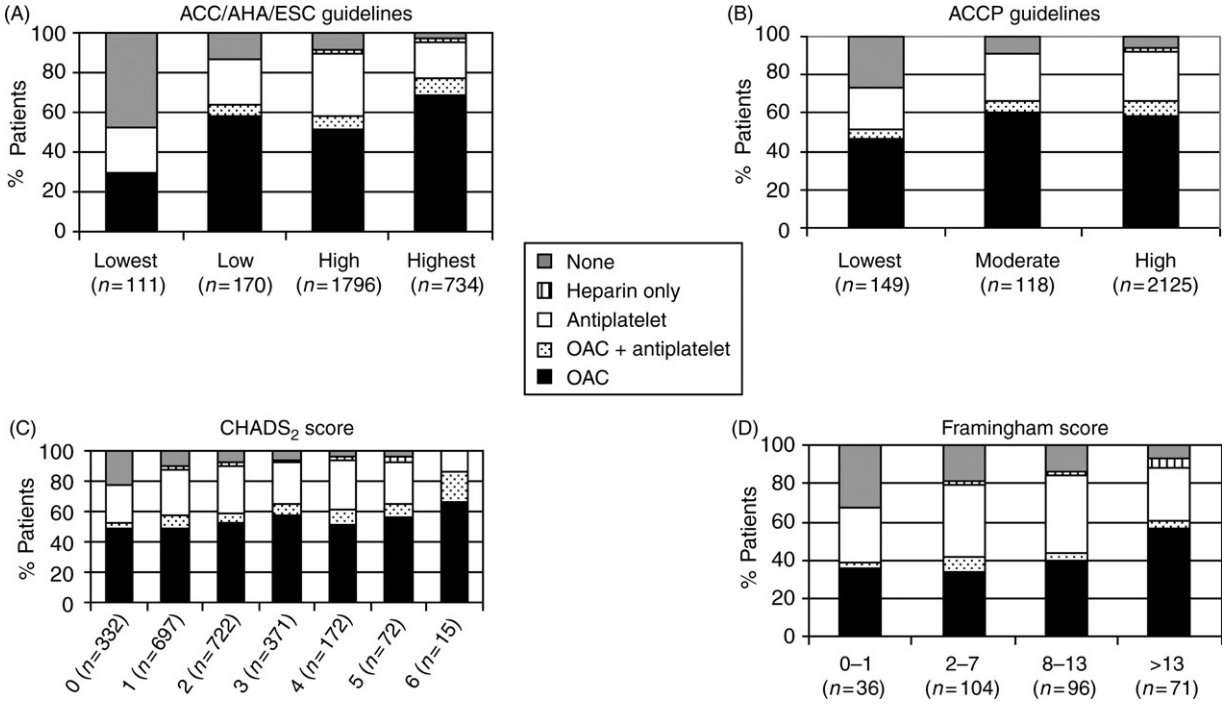

Figure 2 Antithrombotic drug prescription per risk category according to the ACC/AHA/ESC guidelines (*A*), ACCP guidelines (*B*), $CHADS_2$ score (*C*), and the Framingham score (*D*).

Table 2 Factors associated with prescription of OAC

	OR	95% CI	−2 LL	df	*P*-value
Valvular heart disease	5.67	3.83–8.38	106	1	<0.001
AF type (ref. = first detected AF)			141	3	<0.001
Paroxysmal AF	0.87	0.65–1.16			
Persistent AF	2.36	1.68–3.32			
Permanent AF	2.83	2.16–3.71			
Diabetes	1.47	1.17–1.85	11	1	0.001
Reason admission/visit (ref. = AF only)			16	2	<0.001
AF + other reason	0.72	0.58–0.90			
Other reason only	0.63	0.49–0.80			
Major bleeding	0.51	0.29–0.89	6	1	0.019
No OAC monitoring clinic	0.75	0.62–0.91	9	1	0.003
Heart rhythm strategy (ref. = rhythm control)			18	2	<0.001
Rate control	0.99	0.80–1.23			
No rhythm/rate control	0.57	0.42–0.76			

Ref., reference group. Area under the ROC curve = 0.7143.

Table 3 Factors associated with prescription of an antiplatelet drug alone, rather than nothing

	OR	95% CI	−2 LL	df	*P*-value
CAD	4.20	2.87–6.16	63	1	<0.001
Reason admission/visit (ref. = AF only)			16	2	<0.001
AF + other reason	1.92	1.33–2.79			
Other reason only	1.03	0.69–1.55			
Age >75 years	1.65	1.19–2.28	9	1	0.002
Hypertension	1.64	1.20–2.26	9	1	0.002
Malignancy	0.40	0.23–0.72	9	1	0.002
Major bleeding	0.22	0.10–0.48	14	1	<0.001

Ref., reference group. Area under the ROC curve = 0.7366.

Table 4 Factors associated with prescription of a combination of OAC and an antiplatelet drug, rather than OAC alone

	OR	95% CI	−2 LL	df	*P*-value
CAD	4.53	3.29–6.23	93	1	<0.001
No OAC monitoring clinic	1.80	1.31–2.47	13	1	<0.001

Area under the ROC curve = 0.7063.

Table 5 Factors associated with prescription of any antithrombotic drug

	OR	95% CI	−2 LL	df	*P*-value
CAD	3.57	2.43–5.25	51	1	<0.001
AF type (ref. = first detected AF)			68	3	<0.001
Paroxysmal AF	1.02	0.69–1.51			
Persistent AF	2.99	1.69–5.31			
Permanent AF	3.67	2.39–5.64			
Valvular heart disease	3.77	1.86–7.66	19	1	<0.001
Hypertension	1.86	1.38–2.49	17	1	<0.001
Stroke/TIA	2.25	1.24–4.07	7	1	0.008
Major bleeding	0.13	0.07–0.26	25	1	<0.001

Ref., reference group. Area under the ROC curve = 0.7655.

or unknown, and 25% ($n = 106$) when no risk factor was present and AF duration was shorter than 48 h. Among patients who underwent a current ECV, these proportions were, respectively, 86 ($n = 713$), 88 ($n = 122$), 87 ($n = 836$), and 61% ($n = 106$). OAC use around a catheter ablation was high (~80%), and of all patients with at least one risk factor, 92% received OAC. A planned catheter ablation did not trigger OAC prescription, and among these patients, 73% left the hospital protected by OAC.

Discussion

Of contemporary surveys, the Euro Heart Survey did find one of the highest OAC prescription rates in AF patients until now. Nonetheless, the risk of stroke in AF is not homogeneous, and antithrombotic treatment needs to be tailored according to the patient's risk profile. In low-risk patients, OAC provides a minimal benefit in preventing thrombo-embolic strokes when compared with aspirin, which is largely offset by a higher risk of bleedings with OAC. In contrast, high-risk patients undoubtedly benefit from OAC despite the increased bleeding risk.[17–21] Of concern, this survey shows that OAC prescription for AF was quite high throughout all risk categories, irrespective of the stroke risk stratification scheme used, making that a large proportion of low-risk patients is at an avoidable increased hazard for bleeding and troubled with the inconvenience of constant INR monitoring with little chance for benefit.

Application of stroke risk stratification schemes

The ACCP guidelines, and also the Framingham and $CHADS_2$ schemes, have been shown to adequately identify patients at low risk for stroke, whereby the $CHADS_2$ score was superior in identifying patients at high risk.[22] In general, these schemes use the same factors to stratify patients, but the vast majority of patients were classified as high(est) risk in the ACC/AHA/ESC and ACCP schemes and less so with the $CHADS_2$ and Framingham scores. The $CHADS_2$ scheme is probably the most user-friendly tool for physicians to visualize the patient's stroke risk profile, as it is less complex than the Framingham score. However, as there is debate about the importance of accounting uncontrolled hypertension as

Table 6 Characteristics of patients in whom an intervention to restore sinus rhythm was performed or planned

	PCV		ECV		Catheter ablation	
	Performed ($n = 1139$)	Planned ($n = 128$)	Performed ($n = 919$)	Planned ($n = 417$)	Performed ($n = 134$)	Planned ($n = 118$)
Demographics						
Age (years)	64 ± 13	66 ± 10	64 ± 12	65 ± 11	54 ± 11	57 ± 16
Female gender	513 (45)	41 (32)	329 (36)	162 (39)	40 (30)	36 (31)
Duration of current AF episode						
≤48 h	569 (56)	11 (10)	162 (19)	24 (6)		
>48 h	222 (22)	30 (27)	341 (41)	142 (37)		
Unknown duration	219 (22)	69 (63)	333 (40)	216 (57)		
ACC/AHA/ESC risk						
Lowest	101 (9)	4 (3)	77 (8)	25 (6)	46 (35)	22 (19)
Low	82 (7)	10 (8)	110 (12)	26 (6)	19 (14)	15 (13)
High	752 (66)	103 (81)	555 (61)	284 (69)	49 (37)	51 (44)
Highest	199 (18)	11 (9)	173 (19)	79 (19)	18 (14)	29 (25)

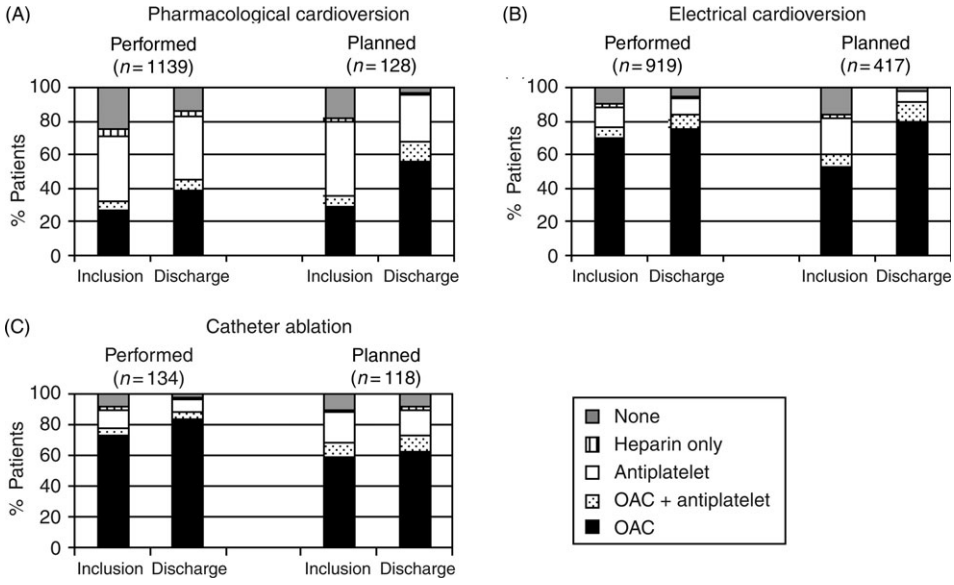

Figure 3 Antithrombotic drug prescription at inclusion and at discharge when the following interventions were either performed at the time of the survey or planned at discharge: PCV (*A*), ECV (*B*), or catheter ablation (*C*).

a stroke risk factor rather than the plain diagnosis of hypertension, the Framingham scheme might be more appropriate on this issue as it includes the actual blood pressure. Until sufficient outcome data clarify this issue, the role of uncontrolled hypertension cannot be denied.

Although the ACC/AHA/ESC and ACCP guidelines give management recommendations according to the risk profile, these recommendations are not yet tailored to the $CHADS_2$ and Framingham scores. Those defined as 'high risk' in all four risk stratification schemes had just a slightly higher chance of receiving OAC or any antithrombotic therapy in general, which was also previously shown for the ACC/AHA/ESC guidelines.[23] Therefore, regardless of the choice for any scheme, antithrombotic therapy prescription seems to be marginally guided by current available stroke risk stratification schemes.

Important factors in the decision-making process regarding antithrombotic treatment

Some generally accepted stroke risk factors were associated with antithrombotic treatment and patients with a prior major bleeding had a lower chance for OAC, both reflecting adequate clinical management. However, several factors that are not generally accepted as stroke risk factors, or that do not have a direct connection with stroke risk, were significantly associated with antithrombotic management decisions. Patients with first detected or paroxysmal AF had a lower chance of receiving OAC compared with patients with persistent or permanent AF, which was in accordance with previous findings.[23] This might relate to the fact that a low AF burden is thought to be associated with a low risk for stroke. Because perceived AF burden is lower in paroxysmal AF patients, historically these patients had a lower chance of receiving OAC than patients with chronic (persistent/permanent) AF. This rationale might still be used in this survey, also because patients not receiving any rhythm or rate control drugs or interventions, in whom perceived AF burden is probably low, have a lower chance of receiving OAC. However, one has to keep in mind that to date there is very limited evidence that a high AF burden is associated with an increased risk for stroke[24,25] and that OAC has been shown to be effective in both paroxysmal (intermittent) and persistent AF patients, although evidence to support this is also quite limited and addressed patients with long-lasting intermittent episodes of AF rather than paroxysmal AF according to the current definition of the guidelines.[26] An important factor complicating this issue is that the physicians' perception of AF burden mostly underestimates the true AF burden, as many patients suffer from asymptomatic recurrences.[27] At the present time, the main focus in this decision-making process should therefore be on the presence of high risk factors for stroke, rather than on the clinical type of AF *per se*.

When AF was the only reason for the qualifying admission or visit, OAC was prescribed more often. This could be due to less distraction by other medical problems or management by an AF specialized physician who is more aware of the importance of OAC. In addition, availability of an OAC monitoring outpatient clinic also played a significant role in the decision-making process. The ability for safe INR monitoring is important for OAC prescription, which is not easy to arrange in all patients and also not in all countries because of restrictions in infrastructure. A (prior) major bleeding was a factor against prescribing any antithrombotic drugs. However, we did not know in detail what kind of bleeding was present, nor how long ago it was diagnosed. Remarkable was the finding that a surprising 40–50% of low-risk patients received OAC. These patients are exposed to an avoidable bleeding hazard, as a platelet inhibitor would suffice in these patients.

When considering the well-known stroke risk factors for which OAC is warranted, logically valvular heart disease played a significant role in the prescription of OAC and to a lesser extent also diabetes. Surprisingly, a (prior) stroke or TIA, but also hypertension and age >75 years were not significantly associated with OAC prescription, and even more remarkable was that heart failure did not play a role in any of the multivariable analyses.

Possible reasons for lack of adherence to stroke risk stratification schemes

Several reasons can underlie the poor application of stroke risk stratification and adherence to antithrombotic treatment guidelines. First, patient factors related to OAC use might contribute to this poor application. Continuing efforts should be made to improve patients' awareness and understanding of the disease process as well as the need for OAC therapy.[28] Secondly, adherence might be poor because of deficiencies in knowledge of the guidelines, but also because of actual deficiencies in the guidelines, which is probably best illustrated by the limited evidence and therefore ongoing debate on the role of clinical type of AF as well as uncontrolled hypertension in stroke risk stratification. Thirdly, some of the four schemes we analysed are complex, whereas if they were presented more simply, they might be better applied. Fourthly, variability exists in weighing the importance of some of the stroke risk factors, with specific dispute whether hypertension alone is an indication and extra dispute for controlled vs. uncontrolled hypertension. Finally, although stroke risk can be estimated in a variety of ways, antithrombotic treatment options are limited to OAC or an antiplatelet agent. Together with the no antithrombotic treatment option, the current therapeutic means as well as the means to risk stratify patients are too limited to tailor treatment properly to the actual stroke risk. Perhaps, new drugs and alternative risk stratification tools, including new imaging modalities, may enhance the use of safe and appropriate antithrombotic treatment in AF.

Combination of OAC and antiplatelet drugs

A combination of OAC and an antiplatelet agent is given in 8% of patients. Little evidence exists for the additive benefit of aspirin to OAC as thromboprophylaxis in AF *per se*, but it increases the risk of bleeding.[29] Physicians still consider this combination as beneficial in vascular disease, but in reality the benefits express mainly in the first 35 days after an acute coronary event, rather than in the long-term.[30] The lower application of combination therapy in the presence of an OAC monitoring clinic might reflect more frequent and strict monitoring of evidence-based antithrombotic drug prescription and confidence that stand alone OAC is adequate even in very high-risk patients.

OAC around interventions for AF

Anticoagulation is recommended for a minimum of 3–4 weeks prior to, and following, cardioversion of AF lasting $>$48 h or with an unknown AF duration; where there is a high risk of AF recurrence or risk factors for stroke, more prolonged anticoagulation after cardioversion is recommended.[3] The low OAC use around PCV in comparison with ECV, even when choosing patients with risk factors or AF of $>$48 h or unknown duration, may reflect physicians' perception that a PCV less urgently warrants stroke prevention therapy than an ECV. In agreement with this is the high OAC use around ECV regardless of stroke risk factors or AF duration. Therefore, attention should be drawn to anticoagulation around PCV and also to tailoring antithrombotic treatment to risk for thrombo-embolism. The ACC/AHA/ESC guideline[2] clearly states that anticoagulation should be given irrespective of the mode of cardioversion; however, the guideline needs rephrasing concerning the need for considering lifelong anticoagulation in case cardioversion patients harbour risk factors for stroke, rather than simply stating that an extended period of anticoagulation might be beneficial. At the time of the survey, no guidelines on antithrombotic therapy around electrophysiological interventions had been implemented, but recently brief recommendations have been published.[31,32] Both papers recommend in patients with moderate to high stroke risk, anticoagulation 3 weeks before the procedure and heparin during the procedure and possibly to cover the transition periods. No recommendation is done considering therapy after the procedure, although experienced research groups report to continue OAC up to 3 months after successful ablation. Therefore, although OAC use seems well implemented around catheter ablation in this survey, clear evidence-based recommendations are warranted.

Clinical implications

Education in the past years on stroke prevention for AF patients has been effective, because cardiologists prescribe antithrombotic therapy in the majority of AF patients who should receive it. However, stroke risk stratification to determine which drug is most appropriate seems scarcely used. Therefore, education should now focus on the importance of tailoring antithrombotic therapy according to the patient's risk profile. To facilitate this tailored treatment, guideline writers and physician educators should focus on providing one uniform and easy to use stroke risk stratification scheme. Extra improvement might be achieved by an information booklet to help improve patient's knowledge about anticoagulation therapy for AF[33] and by integrating stroke risk stratification guidelines in supporting information technology, possibly handled by a specialized nurse. There is still an unmet need for safer and more easy to use antithrombotic drugs, but until this is available the application of OAC according to the presented stroke risk stratification deserves full attention.

Limitations

This cohort does not represent average Europe, as shown in the first report of this survey.[5] The high prescription rate of OAC may relate to the relatively high proportion of university and specialized centres participating. Also, we did not ask the physician what the exact reason was for (not) prescribing antithrombotic treatment, but we report associations of characteristics with this prescription. Finally, the multivariable ORs cannot be considered as true relative risks, as the frequency of OAC prescription was very high.

Acknowledgements

We thank the Euro Heart Survey team, national co-ordinators, investigators, and data collection officers for performing the survey. In addition, we thank the main sponsor AstraZeneca, major sponsor Sanofi-Aventis, and sponsor Eucomed for their support to the Euro Heart Survey on Atrial Fibrillation. Finally, we thank the following institutions for their national support: Austrian Heart Foundation, Austrian Society of Cardiology, French Federation of Cardiology, Hellenic Cardiological Society, Netherlands Heart Foundation, Portuguese Society of Cardiology, Spanish Cardiac Society, and the Swedish Heart and Lung Foundation.

Conflict of interest: none declared.

Appendix: prevalence of risk factors for stroke

Table A1 Prevalence of risk factors for stroke in 5251 patients according to the ACC/AHA/ESC guidelines

Risk category	Prevalence
Lowest	341 (7)
Age <60 years, no heart disease (lone AF)	341 (7)
Low	389 (8)
Age <60 years and heart disease, but no risk factors for stroke	114 (2)
Age ≥60 years and no risk factors for stroke	275 (5)
High	3373 (64)
Age ≥75 years	1086 (21)
Age 60 and <75 years with diabetes or CAD	849 (16)
Heart failure	1230 (23)
Left ventricular ejection fraction ≤0.35	379 (7)
Thyrotoxicosis	Not available
Hypertension	2659 (51)
Highest	1148 (22)
Rheumatic heart disease (mitral stenosis)	323 (6)
Prostethic heart valve[a]	348 (7)
Prior thrombo-embolism	664 (13)
Persistent atrial thrombus on transesophageal echocardiography	Not available

[a]Valve surgery in general.

Table A2 Prevalence of risk factors for stroke according to the ACCP guidelines in 4176 patients with paroxysmal, persistent, or permanent AF

Risk level	Prevalence
Low	395 (9)
Age <65 years, no other risk factors	395 (9)
Intermediate	237 (6)
Age 65–75 years	190 (5)
Diabetes	39 (1)
CAD and left ventricular ejection fraction >0.35	48 (1)
High	3544 (85)
Stroke, TIA, or systemic embolism	555 (13)
Age >75 years	1162 (28)
Moderate or severe left ventricular dysfunction[a]	422 (10)
Congestive heart failure	1473 (35)
Hypertension	2667 (64)
Mitral stenosis	281 (7)
Prosthetic heart valve[b]	315 (8)

[a]Clinical heart failure and/or LVEF ≤0.35.
[b]Valve surgery in general.

Table A3 Prevalence of risk factors for stroke according to the $CHADS_2$ score in 4564 patients with non-valvular AF

	Prevalence
Risk factors	
Congestive heart failure (C)	1458 (32)
Hypertension (H)	3029 (65)
Age ≥75 years (A)	1316 (28)
Diabetes mellitus (D)	831 (18)
History of stroke or TIA (S_2)	473 (10)
Score[a]	
0	828 (18)
1	1526 (33)
2	1244 (27)
3	585 (13)
4	255 (6)
5	103 (2)
6	23 (1)

[a]Congestive heart failure, hypertension, age ≥75 years, and diabetes have score 1 and stroke/TIA has score 2.

Table A4 Prevalence of risk factors for stroke according to the Framingham stroke risk score in 866 patients with newly detected, nonvalvular AF

	Score	Prevalence
Risk factors		
Age (years)		
< 60	0	265 (30)
60–62	1	55 (6)
63–66	2	93 (11)
67–71	3	155 (18)
72–74	4	85 (10)
75–77	5	83 (9)
78–81	6	85 (10)
82–85	7	32 (4)
86–90	8	19 (2)
91–93	9	7 (1)
> 93	10	0 (0)
SBP (mmHg)		
< 120	0	162 (19)
120–139	1	305 (35)
140–159	2	262 (30)
160–179	3	102 (12)
> 179	4	47 (5)
Other factors		
Female gender	6	364 (41)
Diabetes	5	170 (19)
Stroke/TIA	6	61 (7)
Risk category[a]		
Low	0–1	113 (13)
Intermediate	2–7	319 (37)
High	8–13	283 (33)
Highest	>13	151 (17)

SBP, systolic blood pressure.
[a]On the basis of the total score (age + SBP + gender + diabetes + stroke/TIA).

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