Napovedniki antitrombotične terapije pri ambulantnih bolnikih s kronično atrijsko fibrilacijo, ki odstopa od smernic zdravljenja

Predictors for guideline-nonadherence with antithrombotic therapy in outpatients with chronic atrial fibrillation

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Izvleček

Namen: *Razlogi za neustreznost antitrombotičnega zdravljenja pri bolnikih z atrijsko fibrilacijo (AF) so dobro znani. Naši cilj je bil določiti kvaliteto antitrombotičnega zdravljenja pri skupini bolnikov s kronično AF in določiti omejitve ustreznosti antitrombotičnega zdravljenja.*

Metode: *Z multicentričnimi raziskavami smo analizirali podatke o zdravljenju, dejavnikih tveganja za možgansko kap in psihosocialne dejavnike. S pomočjo logistične regresije smo ugotavljali napovedne dejavnike za neustreznost antitrombotičnega zdravljenja, ki odstopa od ustaljenih smernic pri ambulantnih bolnikih s kronično atrijsko fibrilacijo*

Abstract

Purpose: *Our aims were to determine the prevalence of physicians' adherence to antithrombotic guidelines in the management of outpatients with chronic atrial fibrillation (AF) and to identify risk factors for nonadherence to treatment guidelines.*

Methods: *Data on drug treatment, stroke risk factors and psychosocial variables were analyzed descriptively in a cross-sectional community-based multicentre study. Predictors for nonadherence with guidelines for antithrombotic prophylaxis of AF patients were identified using logistic regression.*

Results: *Of 413 outpatients with chronic AF attending the offices of family physicians, 184 (44.6%)*

Rezultati: *Od 413 ambulantnih bolnikov s kronično AF, ki so bili napoteni iz ambulant družinskih zdravnikov, je bilo 184 (44,6%) zdravljenih po priporočenih smernicah (American College of Chest Physicians - ACCP 2001). V skupini bolnikov z visokim tveganjem za možgansko kap (n=387), je bilo 178 bolnikov (46,0%) zdravljenih po smernicah. 31 bolnikov z visokim tveganjem je prejelo kumarinsko terapijo, čeprav je bila pri njih prisotna vsaj ena kontraindikacija. Multivariantna analiza je pokazala, da je prisotnost absolutne kontraindikacije za kumarin neodvisni napovednik za zdravljenje, ki odstopa od smernic.*

Zaključek: *Za izboljšanje priporočenih smernic antitrombotičnega zdravljenja ambulatnega bolnika z AF, je dejavnike tveganja potrebno upo'tevati za vsakega bolnika posebej.*

were treated according to the American College of Chest Physicians (ACCP) 2001 guidelines. In the group of patients with a high risk of stroke (n=387), 178 patients (46.0%) received guideline-adherent treatment. 31 of the high-risk patients received coumarin although they had at least one contraindication. Multivariate analysis showed the presence of absolute contraindications to coumarins to be an independent predictor of guideline-nonadherent treatment.

Conclusion: *To improve guideline-adherence in the antithrombotic treatment in AF outpatients, strategies involving individual assessment of the risks and benefits will need to be established and implemented.*

INTRODUCTION

Atrial fibrillation (AF) is associated with a substantial increase in morbidity and mortality, with stroke being the most serious complication. To prevent thromboembolic events, adjusted-dose treatment with coumarin-type oral anticoagulants (e.g., warfarin or phenprocoumon) is the mainstay of antithrombotic treatment in AF patients with moderate to high risk of stroke. Aspirin is reserved for patients at lower stroke risk or for higher-risk patients with contraindications to coumarins (1).

Although current treatment guidelines recommend adjusted-dose oral anticoagulants for the majority of AF patients (2-5) and health outcome studies support the effectiveness of this strategy (6-10), observational studies show that anticoagulant therapy is still substantially underused or inappropriately used thus imposing preventable risks of thromboembolism on AF patients (11-15). Predictors of guideline nonadherence, however, are largely unknown.

We analyzed the antithrombotic therapy of a cohort of AF outpatients and assessed individual stroke risk, potential contraindications to coumarins and aspirin, and the appropriateness of stroke prophylaxis according to the 2001 guidelines of the American College of Chest Physicians (ACCP) (2) and identified predictors of guideline nonadherence.

MATERIAL AND METHODS

Setting and study design

Full details of the method have been described in a previous article (16). In brief, all family physicians in the study regions were invited to participate as study centers. This target group included all primary-care doctors and specialists in internal medicine with a family medicine focus registered with the regional Physicians in Public Health Insurance Board (Kassenärztliche Vereinigung).

The study region included districts within the state of Baden-Württemberg, Southern Germany, with urban (Tübingen, Reutlingen, Freiburg, Offenburg) and surrounding rural areas.

Participating physicians submitted a list of their patients diagnosed with chronic AF, i.e. an ICD-10 code of I48 or I49.8, to the Division of Clinical Pharmacology at the University Hospital Tübingen (the steering center).

If a physician reported having more than 10 AF patients, the steering center randomly selected 10 patients from among them. The limit of 10 patients was set to avoid over-representation of single offices and their policies in AF management.

Patients from 18 to 85 years were included if chronic non-valvular AF was diagnosed. Chronic AF included recurrent (intermittent) AF, defined as two or more episodes of AF, or permanent AF (17). A physician at the steering center re-analyzed a recent electrocardiogram (ECG) from each potential study patient to confirm the diagnosis of AF.

The exclusion criteria were another condition requiring oral anticoagulation (e.g., pulmonary embolism, mitral stenosis, prosthetic heart valve); being scheduled for cardioversion, electroablation or cardiac surgery in the next 4 weeks; having a life expectancy of less than 1 year; or being unable to give informed written consent for study participation.

The ethical committees of the Medical Faculty of the University of Tübingen and of the Physicians' Chamber (Landesärztekammer) Baden-Württemberg approved the study protocol. The authors certify that all applicable institutional and governmental regulations covering the ethical use of human volunteers were followed during this research.

Target variables

The primary target variable was the percentage of enrolled patients whose antithrombotic treatment was compatible with the ACCP 2001 recommendations (2,18) (Figure 1). These guidelines were used because they were state of the art when the study was initiated in 2003.

On two occasions physicians at the steering center assessed whether each patient's management adhered to the guidelines by comparing data from the case report form (CRF) with the text of the reference ACCP guidelines. In addition, a computerized decision algorithm was used (Figure 1). If the physicians and computer assessment results differed, guideline adherence was re-assessed by the steering center. Cases where there was no detectable difference between the care being offered and the recommendations of the guidelines were judged to be compliant with guidelines.

Secondary target variables included the following quality indicators: percentage of high-risk patients receiving a coumarin anticoagulant; anticoagulation level within the target INR range of 2.0-3.0; and whether the results of an echocardiogram were made available.

To find predictors of inappropriate antithrombotic treatment, 47 potential variables (including physicians' specialization and patients' demographic characteristics, medical history, concomitant medication, ischaemic and bleedings risks, and social data) were selected from the findings of previous observational studies (see sections B and C of Table IV for the most important variables). Univariate analysis of the data was performed. Factors found to have a predictive potential by univariate analysis ($p<0.1$) were selected to undergo multivariate analysis. Variables predicting a high risk that AF patients would receive inappropriate antithrombotic treatment were identified by the multivariate analysis.

Data acquisition

Participating physicians completed a CRF with 124 variables for each patient. The variables included current health status, medication, various thromboembolic and haemorrhagic risk factors, and psychosocial variables, such as mental and physical activity, family situation and compliance.

Generally accepted contraindications to antithrombotic agents are listed in Table I. The table

Figure 1: *Algorithm to decide on the adherence of antithrombotic treatment to the ACCP 2001 guidelines (2) in study patients with chronic AF.*

Step 1: Estimation of stroke risk if given aspirin2,18

Annual stroke risk	Low (<2%)	Moderate (2-4%)	High (>4%)
Risk factors for thromboembolism	• Age <65 years • No clinical or echocardiographic symptoms of cardiovascular disease	Only one of the following features: • age 65-75 years • diabetes mellitus • coronary artery disease without signs of heart failure	• age >75 years • stroke, TIA or systemic embolus • history of hypertension • poor left ventricular systolic function (clinical or echocardiographic features of systolic heart failure, NYHA class >1) • mitral valve disease, prosthetic heart valve • presence of >1 moderate risk factors

Step 2: Identification of risk factors for major bleeding (Table I)

- Determination of number and kind of absolute or relative contraindications to coumarins,
- Determination of number and kind of absolute contraindications to aspirin.

Step 3: Determination of the appropriate antithrombotic treatment, recommended by the ACCP 2001 guidelines (2) in 4 scenarios:

Scenario	1. No absolute contraindication to coumarins or aspirin			2. One or more absolute contraindications to coumarins			3. One or more absolute contraindications to aspirin			4. Absolute contraindications to aspirin and to coumarins		
Risk level	high	moderate	low	high	moderate	low	high	moderate	low	high	moderate	low
Recommended therapy	coumarin INR 2.0-3.0	aspirin 325 mg/d or coumarin INR 2.0-3.0	aspirin 325 mg/d	aspirin 325 mg/d	aspirin 325 mg/d	aspirin 325 mg/d	coumarin INR 2.0-3.0	coumarin INR 2.0-3.0	n.a.	n.a.	n.a.	n.a.
Levels of evidence*	1A	1A	2C	1A	1A	2C	1A	1A				

In patients with only relative contraindications to coumarins, recommendations of scenario 1 were used. When treatment of high-risk patients with relative contraindications did not correspond to the guidelines, the clinical significance of these barriers was evaluated on an individual basis.

Step 4: Comparison of the existing antithrombotic treatment with the recommendations of the ACCP 2001 guidelines (2)

If a patient's antithrombotic agent, its daily dose, and INR is according to stroke risk, bleeding risk, and the treatment option as proposed by the guidelines,	If a patient's antithrombotic agent, its daily dose, or INR differs from guideline recommendations,	If a patient has • absolute contraindications to both aspirin and coumarins or • absolute contraindications to coumarins but more than 2 high-risk factors for thromboembolism (ACCP 2001 guidelines do not provide explicit recommendations for such situations) ("borderline situations")
↓	↓	↓
this patient's treatment is considered as **guideline-adherent**	this patient's treatment is considered as **not guideline-adherent (nonadherence)**	this patient's treatment is considered as **guideline-adherent**

* as indicated by Guyatt et al(28).

Table I: *Presence of contraindications to coumarins or aspirin in 413 patients with chronic AF*
The contraindications are derived from the summary of product characteristics.
Some patients had more than one contraindication.

Contraindication	N
Absolute contraindications to coumarins. The presence of at least one of the following variables precludes the use of a coumarin.	
Severe haematoma after oral anticoagulation	12
Current faecal or urinary microbleeding	12
Other bleeding episodes after oral anticoagulation requiring medical intervention	11
Chronic use of an NSAID	10
Hepatic disease and alcohol abuse	7
Vascular malformation posing a bleeding risk	7
History of proliferative diabetic retinopathy	7
History of intracranial hemorrhage or recent CNS surgery	5
Gastrointestinal or genitourinary bleeding during the preceding 6 months	3
Hypersensitivity to or intolerance of coumarins	3
Active peptic ulcer	2
Thrombocytopenia (<100,000 µl-1)	2
Systolic blood pressure >180 mm Hg or diastolic blood pressure >95 mm Hg	3
Severe renal dysfunction (serum creatinine >3.0 mg/dl)	0
Total of absolute contraindications to coumarins	**81**
Relative contraindications to coumarins. If one of the following variables is present, oral anticoagulation may be withheld in AF patients at an intermediate or low risk of stroke, as defined by the ACCP 2001 guidelines (2).	
Alcohol abuse (without hepatic disease)	24
Hepatic disease (without alcohol abuse)	20
Dementia	23
Poor patient compliance (as indicated by the physician)	17
Falls in the preceding 12 months	16
Decline of anticoagulant therapy by the patient	8
Total of relative contraindications to coumarins	**116**
Absolute contraindications to aspirin	
Hypersensitivity to or intolerance of aspirin or NSAIDs	4
Active peptic ulcer	2
Haemorrhagic diathesis or thrombocytopenia (<100,000 µl-1)	2
Total of absolute contraindications to aspirin	**8**

reflects the exclusion criteria used in the SPAF I-III and SPINAF trials (19-23) and in the summaries of the product characteristics (24) of phenprocoumon as indicated in the written product material provided by the manufacturers (e.g., Marcumar®).

Anticoagulation intensity was assessed using the results of the most recent test of the international normalized ratio (INR) by the participating physician. A specialist in internal medicine at the steering center assessed left ventricular function using clinical and echocardiographic documents, if available.

Table IV: *Factors with the potential to predict guideline nonadherence in antithrombotic management (from 387 chronic AF outpatients at a high risk of stroke).*
The relative risk (risk ratio, RR, with confidence intervals, CI) for factors predicting guideline nonadherence and the p values were estimated using univariate analysis. For factors found to have no predictive value (p>0.1), no RR is given (section C). Factors found to have a predictive potential (p<0.1; section B) were selected to undergo multivariate analysis. One of these factors, namely, "having an absolute contraindication to coumarins", was found to be a predictor in multivariate analysis (section A).

Factor	RR (95%-CI)
A) Predicting nonadherence by multivariate analysis (adjusted RR)	
Having an absolute contraindication to coumarins (Table I)	51.73 (6.82–392.58)
B) Predicting nonadherence by univariate analysis: p<0.1	
Treatment by a general practitioner	1.23 (0.98–1.54)
Having no echocardiogram performed	1.32 (1.08–1.60)
Having diabetes mellitus	1.22 (1.01–1.47)
History of non-life-threatening bleeding	1.59 (1.31–1.93)
Having a relative contraindication to coumarins (Table I)	1.40 (1.15–1.69)
History of falls	1.33 (1.07–1.64)
Needing assistance to see the doctor	1.37 (1.11–1.69)
Barthel Index* score <95	1.29 (1.03–1.62)
Having at least one absolute contraindication to coumarin use (Table I)	2.14 (1.89–2.42)
C) Variables not predicting nonadherence: p>0.1 in univariate analysis	
Male sex	
Age >75 years	
Body mass index	
AF duration >5 years	
Permanent or intermittent AF	
Regular daily use of >5 drugs	
History of heart failure	
History of hypertension	
Presenting with systolic blood pressure >140 mm Hg and/or diastolic blood pressure >90 mm Hg	
History of heart valve disease	
History of stroke or thromboembolism	
History of hyperthyroidism	
History of coronary heart disease including myocardial infarction, stable angina, bypass surgery or angioplasty	
Alcohol abuse	
Vascular malformations	
History of cerebral or other severe haemorrhage	
HbA1C >6.5% in diabetic patients	
Fasting blood glucose >130 mg/dL	

* The Barthel Index reflects functional abilities in daily life on a scale of scores ranging from 0 to 100. It includes variables such as ambulation, stair climbing, transfers, personal hygiene, feeding, excretion and dressing. A score of 95 was chosen as a cut-off for a reduced Barthel Index.

Upon submission of a CRF to the steering center, completeness and plausibility were checked and any issues were clarified with the study centers. Data were entered into an electronic database on two separate occasions by different investigators (double entry).

Data analyses

The statistical analysis involved all study patients and was made for descriptive purposes. Continuous variables are expressed as mean values +/- standard deviations or as median and quantiles, depending on their distribution. Discrete variables are expressed as counts and percentages.

For identifying barriers to guideline adherence, univariate Mantel-Haenszel statistical analyses, presenting p-values and relative risks for potential barrier factors, were performed. These factors were chosen a priori (Table IV) and were believed to have potential effects on the rate of guideline adherence. Next, a multivariate logistic regression for the primary outcome was performed. The model includes all variables with missing values in the CRFs of less than 10% of patients and includes a minimum of 5% of patients remaining in the risk group (risk for nonadherence) of the respective variable . The final model was the result of a stepwise backward procedure based on the full model, which included every barrier factor with an entry level of $p<0.1$. The results of the logistic regression are presented with p-values and odds ratios with 95% confidence intervals. The SAS software package version 8.0 for Windows (SAS Institute, Cary, NC) was used for the statistical analysis.

Contraindications to antithrombotic drugs

Absolute contraindications to coumarins or aspirin (Table I), such as an active peptic ulcer or chronic use of non-steroidal anti-inflammatory drugs, justified withholding anticoagulation treatment with a coumarin.

Relative contraindications include dementia, poor compliance, and alcohol abuse without hepatic disease. The clinical significance of these relative contraindications to coumarins is highly variable among patients and can be assessed only on an individual basis. We therefore accepted any antithrombotic treatment for these patients as being guideline-adherent.

RESULTS

1022 patients with chronic AF were reported to the steering center by a total of 94 local study centers (Figure 2) between July 2001 and June 2003. From these 1022 patients, the steering center randomly selected 510 patients. From this group, 97 patients were excluded for various reasons (details in Figure 2), with the absence of confirmation of AF (43 patients) and the presence of other conditions requiring anticoagulant therapy

Figure 2: *Flow diagram of patient identification, inclusion and analysis.*

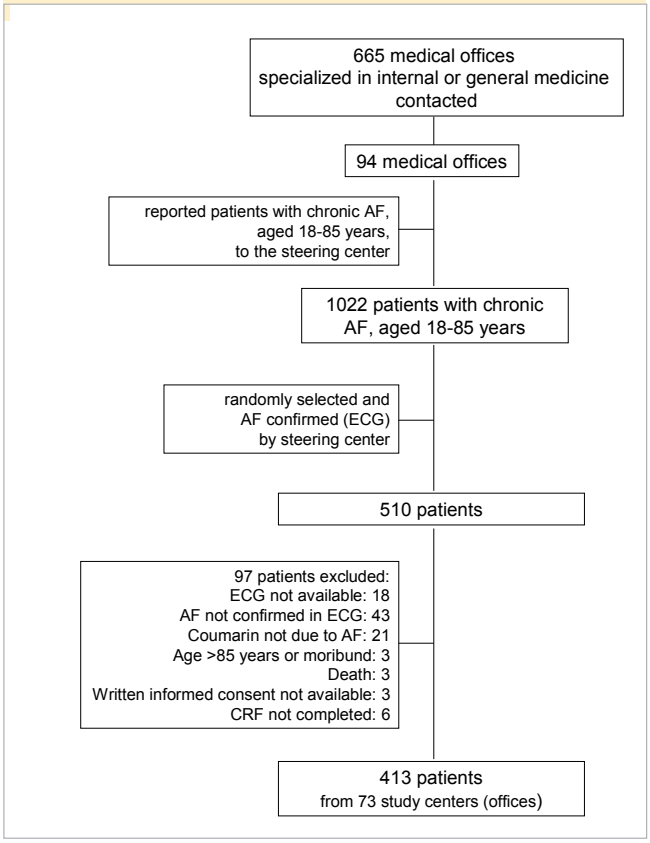


Table II: *Patient characteristics (N=413)*

	Number (%)
Demographic characteristics	
Age <65 years	66 (16.0)
Age >75 years	182 (44.1)
Male gender	231 (55.9)
Clinical characteristics	
Type of chronic AF: -recurrent (intermittent) AF -chronic AF	 62 (15.0) 351 (85.0)
History of hypertension	281 (68.0)
Congestive heart failure functional class NYHA II-IV	185 (44.8)
Reduced systolic left ventricular function in EC (performed in 179 patients)	81 (45.3)
Diabetes mellitus	126 (30.5)
Coronary heart disease History of myocardial infarction History of coronary artery bypass grafting surgery or angioplasty	98 (23.7) 41 (9.9) 26 (6.3)
History of ischaemic stroke or TIA	92 (22.3)
Valvular heart disease	67 (16.2)
History of non-cerebral embolism (pulmonary embolism, deep venous thrombosis, peripheral arterial embolism)	60 (14.5)
History of hyperthyroidism	22 (5.3)
Thromboembolism risk groups according to ACCP 2001 guidelines (2)	
High risk	387 (93.7)
Intermediate risk	14 (3.4)
Low risk	12 (2.9)
Coumarin treatment	302 (73.1)
Psychosocial characteristics	
Alcohol abuse or other addiction	24 (5.8)
Dementia (as indicated by the family doctor)	23 (5.6)
Barthel Index of activities of daily living Severely reduced (≤70) Not impaired (>95)	 14 (3.4) 361 (87.4)
Living alone at home	104 (25.2)
Living in institutionalized care (nursing home, old people's home, care at home by a welfare agency)	14 (3.4)
Needing assistance to see the physician or requiring home visits	52 (12.6)

(21 patients) being the most frequent reasons for exclusion. Eventually, 413 patients from 73 study centers were enrolled.

Patient characteristics

The mean (+/- SD) age was 73.0 (8.1) years (median, 74.0 years). 347 (84.1%) patients were ≥65 years old. 44.1% of the patients were 76 to 85 years old (Table II). All patients were of Caucasian origin. 351 (85.0%) patients had a history of chronic AF.

387 (93.7%) of the enrolled patients had a high risk (i.e., ≥4% per year) of systemic thromboembolism (Figure 1, step 1). The most frequently encountered risk factors were a history of hypertension (68.0%),

Table III: *Indicators for the quality of antithrombotic therapy in 413 outpatients with chronic AF.*

	Number (%)
Guideline-adherent antithrombotic therapy given to	
All patients* (N=413)	184 (44.6)
a) patients at high risk of stroke (N=387)	178 (46.0)
b) patients at intermediate risk of stroke (N=14)	5 (35.7)
c) patients at low risk of stroke (N=12)	1 (8.3)
Other quality indicators	
ECG performed	179 (43.3)
Oral anticoagulation with a coumarin	297 (71.9)
INR of patients on a coumarin (N=297) INR in target range (2.0–3.0) INR <2.0 INR >3.0 no INR available INR test not older than 4 weeks	 208 (70.0) 53 (17.8) 25 (8.4) 11 (3.7) 240 (80.8)
Patients on a coumarin also receiving aspirin	2 (0.7)

* This group includes 11 patients with unique combinations of clinical conditions: 9 had both risk factors for stroke and for haemorrhage and 2 patients with active peptic ulcer and thrombocytopenia (platelet count <100,000 µl-1) had absolute contraindications to both aspirin and coumarins. Appropriateness of antithrombotic treatment in such patients cannot be assessed on the basis of the ACCP guidelines (2).

congestive heart failure (44.8%), age >75 years (44.1%), diabetes mellitus (30.5%) and coronary heart disease (23.7%) (Table II). A history of hyperthyroidism was recorded in 22 (5.3%) patients.

Patients receiving coumarin treatment

Of the 413 patients analyzed, 297 (71.9%) were on coumarin treatment. Of patients at a high risk of stroke, 283 (73.1%) were treated with a coumarin. Among the 334 high-risk patients eligible for coumarin therapy, 248 (74.3%) actually did received it (Figure 3).

Contraindications to antithrombotic drugs

104 (25.2%) patients had at least one contraindication to coumarin or aspirin, with 54 (13.1%) patients having at least one absolute contraindication to coumarins, even given a high risk of thromboembolism . For these patients, the ACCP 2001 guidelines recommend the use of aspirin 325 mg daily.

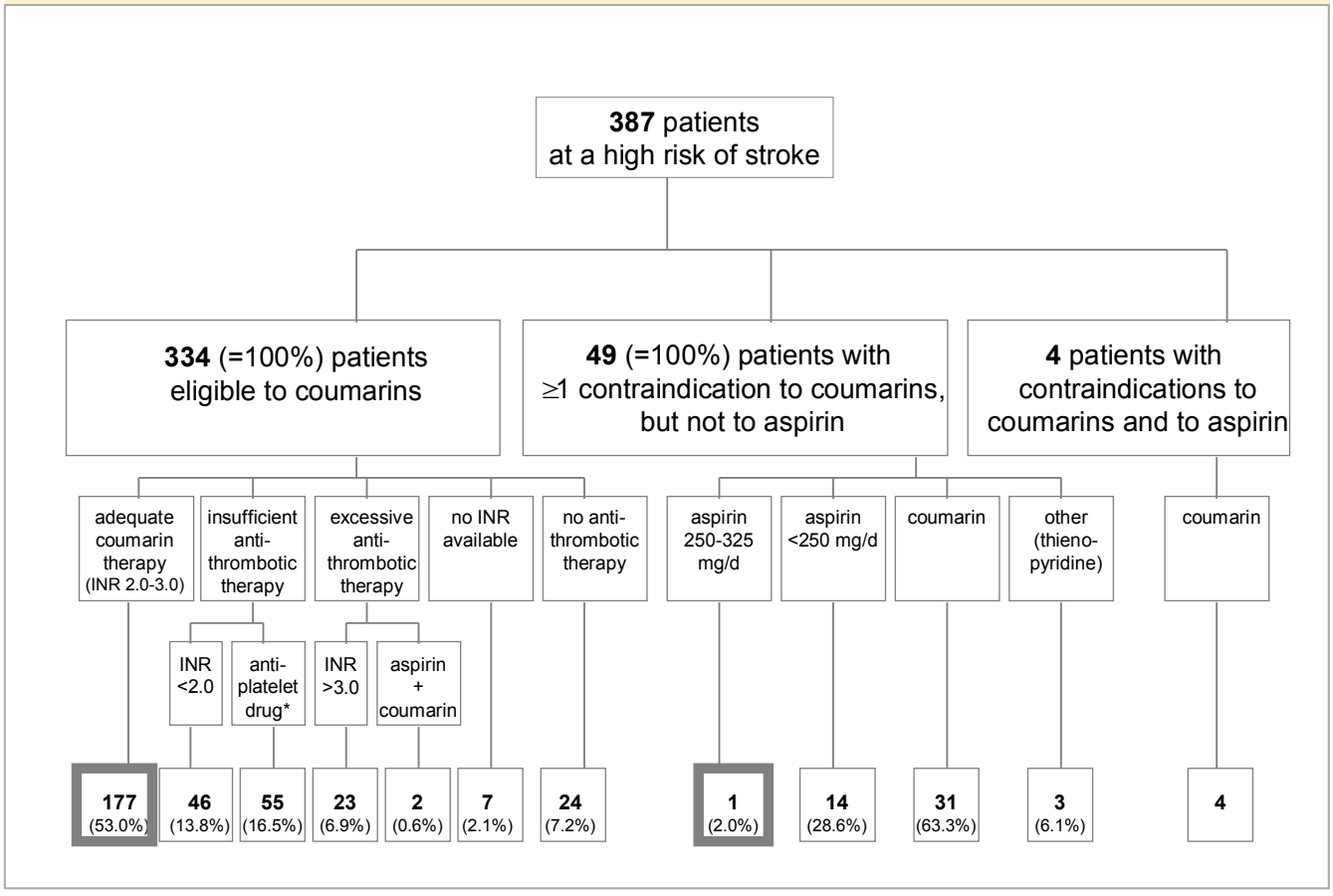
Only five patients had absolute contraindications to aspirin. Four of these patients had active peptic ulcers and thrombocytopenia (<100,000 µl-1), respectively , and were not eligible for a coumarin as an alternative drug. As no recommended alternative treatments for these situations are available, the antithrombotic treatment of these patients was accepted as being appropriate.

Overall guideline adherence

302 (73.1%) patients received a coumarin (Table II). Ten patients were prescribed a thienopyridine (clopidogrel or ticlopidine) with or without concomitant aspirin. One patient received enoxaparin. Two patients received a combination of aspirin plus phenprocoumon. 31 (7.5%) patients were on no antithrombotic agent at all.

Only 184 (44.6%) patients were treated according to the recommendations of the 2001 ACCP guidelines (Table III). Of all 387 patients (93.7%) with a high

Figure 3: *Antithrombotic treatment in the group patients at high-risk of stroke.*
Bold frames: Treatment as recommended by the 2001 ACCP guidelines (2). 178 patients of this group received antithrombotic treatment according to the guidelines.



risk of stroke, only 178 (46.0%) were treated according to the guidelines (bold frame in Figure 3).

Guideline adherence in AF patients with a high risk of stroke

Of the 387 high-stroke-risk patients, 334 were eligible for coumarin treatment. However, only 177 patients (53.0%) in this group both received it and were in the target INR range (2.0–3.0) (Figure 3). Guideline violations were found in 157 coumarin-eligible patients. Of these, 46 patients (13.8%) were on coumarin treatment with an INR <2.0, 55 patients (16.5%) received an antiplatelet drug or enoxaparin instead of a coumarin, and 24 patients (7.5%) were on no antithrombotic therapy whatsoever. The INR was unavailable in 7 patients (2.1%). Excessive treatment was found in 25 cases: 23 coumarin patients had an INR >3.0 and 2 patients were on a coumarin and aspirin concomitantly.

Forty-nine high-stroke-risk patients had at least one absolute contraindication to coumarin treatment. The right therapy, namely, a correct dose of aspirin (250–350 mg/d), was prescribed to only one patient (bold frame in Figure 3). However, in the majority of cases (31 patients, 63.3%), patients received a coumarin despite their absolute contraindication and against the recommendations of the guidelines; furthermore, two of these patients had an INR >3.0. The dose of aspirin was too low in 14 patients (28.6%). Three patients were on a thienopyridine antiplatelet drug. Four patients who had a contraindication to both coumarins and aspirin nevertheless received a coumarin.

Guideline adherence in AF patients with an intermediate risk of stroke

Fourteen patients had an intermediate risk of stroke (Table III). Of these, five patients received guideline-adherent treatment (4 coumarin, 1 aspirin). There were, therefore, nine guideline violations: two patients were on aspirin <250 mg/d , three patients were on a coumarin and had an INR <2.0 (in one case despite the presence of a contraindication to coumarin use) and three patients received no antithrombotic treatment.

Guideline adherence in AF patients with a low risk of stroke

Among the 12 low-stroke-risk cases (Table III), one patient was on a correct dose of aspirin. Of the other 11 cases, three were on aspirin <250 mg/d and four were on a coumarin while four received no antithrombotic therapy .

Second-line quality indicators of antithrombotic management

297 patients from the total study population received a coumarin. 208 (70.0%) had recent INR test results within the target range of 2.0 to 3.0. However, 17.8% of the INR test results were subtherapeutic (INR <2.0) (Table III). Echocardiography had been performed in 179 (43.3%) patients.

Predictors of inappropriate antithrombotic therapy in AF patients

From 47 variables, nnine (Table IV, section B) were identified by univariate analysis ($p<0.1$) as potential predictors of inappropriate antithrombotic treatment in AF patients with a high risk of stroke. Following subsequent multivariate analysis of these nine variables, one turned out to be associated independently with nonadherence to the 2001 ACCP guidelines, namely, having one or more absolute contraindications to oral anticoagulant use (Table IV, section A).

DISCUSSION

We found that less than half of high-risk patients received adequate treatment.

Underuse of anticoagulant treatment in patients with chronic AF has been investigated by several authors. They found rates of anticoagulation of 20% (25), 27% (13), 45% (26), 50.4% (12) or 23% to 31% (9), respectively, with the variability of the rates being due to the differing settings of the studies. In one survey, more than 90% of 312 office-based physicians reported to regularly prescribe a coumarin to AF patients (27). In view of these rates, our finding of 71.9% of AF patients on a coumarin seems to be favourable.

However, further analysis showed that crude anticoagulation rate appears to be an insufficient indicator of quality. This is because in substantial numbers of coumarin patients therapy was either inadequate (INR out of the target range, INR unavailable or concomitant antiplatelet therapy) or contraindicated. In fact, having a contraindication to coumarin therapy predicted guideline nonadherence. This overuse of coumarins is the major finding that the present study adds to current knowledge.

A limitation of our study may be a potential selection bias. Physicians who chose to participate may be more aware of guidelines than others who declined, and overall guideline nonadherence rates may therefore have been underestimated.

Guideline adherence was analysed against the ACCP guidelines of 2001 because they were the most recent ones at the time of use. The ACCP guidelines were updated in 2004 (3) and new guidelines for the management of patients with AF were also published by the American College of Cardiology (ACC), American Heart Association (AHA) and European Society of Cardiology (ESC) in 2006 (29). Using these two newer guidelines, 45.5% (ACCP) (3) or 54.2% (ACC/AHA/ESC) (29), respectively, of our patients received guideline-adherent antithrombotic treatment. This is not fundamentally different from

our finding using the 2001 ACCP guidelines. Additionally, the ACCP published new guidelines in 2008; essentially, they recommend aspirin at a dose of 75 to 325 mg/d for low-risk patients (30).

In conclusion, efforts should be directed to improving guideline implementation. Improved communication of guidelines will be needed. On a physician-patient level, a management algorithm may be help clinicians select appropriate individualized antithrombotic treatment. Currently, the variety of types of software used in physicians' offices makes implementing an electronic decision support system, including alert signals, difficult. The present data illustrate that every AF patient needs individual assessment of the risk of stroke and risk of bleeding. This analysis is complex and many factors need to be taken into account.

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Abbreviations:

ACCP	- American College of Chest Physicians
AF	- atrial fibrillation
CRF	- case report form
EC	- transthoracic echocardiogram
ECG	- electrocardiogram
INR	- international normalized ratio
NSAID	- nonsteroidal anti-inflammatory
NYHA	- New York Heart Association functional class
TIA	- transient ischaemic attack

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