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Albert L. Waldo, Richard C. Becker, Victor F. Tapson, Kevin J. Colgan, for the NABOR Steering Committee

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Hospitalized Patients With Atrial Fibrillation and a High Risk of Stroke Are Not Being Provided With Adequate Anticoagulation

Albert L. Waldo, MD,* Richard C. Becker, MD,† Victor F. Tapson, MD,‡ Kevin J. Colgan, MA,§ for the NABOR Steering Committee

Cleveland, Ohio; Durham, North Carolina; and Oak Brook, Illinois

OBJECTIVES The purpose of this study was to determine both treatment gaps and predictors of warfarin use in atrial fibrillation (AF) patients enrolled in a national multicenter study.

BACKGROUND The National Anticoagulation Benchmark Outcomes Report (NABOR) is a performance improvement program designed to benchmark anticoagulation prophylaxis, treatment, and outcomes among participating hospitals.

METHODS A retrospective cohort study of inpatients was performed at 21 teaching, 13 community, and 4 Veterans Administration hospitals in the U.S. Patients with an ICD-9-CM code for AF (427.31) were randomly selected.

RESULTS Among the 945 patients studied, the mean age was 71.5 (± 13.5) years; 43% were >75 years of age, 54.5% were men, and 67% had a history of hypertension. Most (86%) had factors that stratified them as at high risk of stroke, and only 55% of those received warfarin. Neither warfarin nor aspirin were prescribed in 21% of high-risk patients, including 18% of those with a previous stroke, transient ischemic attack, or systemic embolic event. Age >80 years ($p = 0.008$) and perceived bleeding risk ($p = 0.022$) were negative predictors of warfarin use. Persistent/permanent AF ($p < 0.001$) and history of stroke, transient ischemic attack, or systemic embolus ($p = 0.014$) were positive predictors of warfarin use, whereas high-risk stratification was not.

CONCLUSIONS This study confirms the under-use of warfarin, but also adds to published reports in several regards. It showed that risk stratification, the guidepost for treatment in international guidelines, had little effect on warfarin use, and that age >80 years and AF classification (permanent/persistent) are factors that influence warfarin use. (J Am Coll Cardiol 2005;46: 1729–36) © 2005 by the American College of Cardiology Foundation

Stroke is one of the leading causes of adult disability in the U.S. Presently there are 4.7 million stroke survivors living in the U.S., with 15% to 30% of those being permanently disabled. Stroke costs the U.S. $31 billion in direct costs and $20.2 billion in indirect costs annually. (1).

Atrial fibrillation (AF) is a strong, independent risk factor for stroke because it is associated with formation of left atrial thrombi. With advancing age, AF becomes an increasingly important cause of stroke, with a prevalence <1% in those less than 60 years old and 8% to 10% in those more than 80 years of age (2–4). Each year, 60,000 strokes occur among 2.3 million Americans with this arrhythmia and consequential risk for stroke and systemic emboli. These incidences are predicted to more than double in the coming decades (5). Randomized, controlled trials (6–13) have shown that anticoagulation with warfarin (international normalized ratio [INR], 2 to 3) reduces the risk of ischemic stroke by about 68% in unselected patients with AF (14–16).

This study was performed to determine recent stroke prevention practices, including predictors of anticoagulation utilization, for inpatients with a primary or secondary diagnosis of AF. In addition, benchmarking was used to provide a stimulus for improving antithrombotic management in hospitals, where needed.

METHODS

Patient selection. Patients included in this study were from hospitals participating in the National Anticoagulation Benchmark and Outcomes Report (NABOR) program (EPI-Q Inc., Oak Brook, Illinois). The NABOR was designed to evaluate anticoagulation practices among U.S. hospitals and to provide benchmark data on performance indicators from which participating hospitals could develop a quality improvement strategy for antithrombotic therapy. Seventy-five hospitals were invited to participate in the NABOR program, and the first 40 hospitals responding were selected. Potential participants were identified based on referrals from professional societies, and also by random selection by region. Hospitals were classified as academic, community, or Veterans Administration (VA) facilities. Those with a disproportionate share designation, based on

From the *Division of Cardiology, Case Western University/University Hospitals of Cleveland, Cleveland, Ohio; the †Duke Clinical Research Institute, Durham, North Carolina; the ‡Department of Pulmonary Medicine, Duke University Medical Center, Durham, North Carolina; and §EPI-Q Inc., Oak Brook, Illinois. This study was supported in part by an unrestricted grant from AstraZeneca, LLP. AstraZeneca had no role in the design or conduct of the study; nor in the collection, management, analysis, or interpretation of the data; nor in the preparation, review, or approval of this manuscript. Dr. Waldo is a consultant to AstraZeneca; Dr. Becker is a consultant to AstraZeneca; Dr. Tapson is a consultant to AstraZeneca and Aventis; Mr. Colgan is a consultant to AstraZeneca.

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Abbreviations and Acronyms

AF = atrial fibrillation
AFASAK = Atrial Fibrillation Aspirin and Anticoagulation study
BAATAF = Boston Area Anticoagulation Trial for Atrial Fibrillation
CAFA = Canadian Atrial Fibrillation study
EAFT = European Atrial Fibrillation Trial
INR = international normalized ratio
NABOR = National Anticoagulation Benchmark and Outcomes Report
SPAF = Stroke Prevention in Atrial Fibrillation study
SPINAF = Stroke Prevention in Nonrheumatic Atrial Fibrillation study
TIA = transient ischemic attack
VA = Veterans Administration

their providing care to a high proportion of patients receiving Medicare or Medicaid supplemental security income, were also identified. Because no personal health information was collected, institutional review board approval versus exemption was determined by individual participating hospitals.

Lists of patients meeting inclusion criteria were generated by each participating center for the study period of January 1, 2002, through December 31, 2002. From these lists, 25 records from each participating center were selected randomly for inclusion. One site was allowed to include patients treated beginning in July 2000 to obtain the requested number of records for that site.

Eligibility. Patients' records were eligible for inclusion in the NABOR program based on ICD-9-CM codes after discharge. Included were patients discharged with a primary or secondary diagnosis of AF (ICD-9-CM 427.31). Patients were excluded if they were <18 years old, were admitted from another acute care hospital where therapy was already initiated, or were discharged to another acute care hospital to continue treatment.

Data collection. Patients admitted in the target population had charts reviewed by hospital personnel to determine the following: demographics; risk factors on admission predisposing patients to bleeding or thromboembolic events; therapy for prevention and treatment of thromboembolic and ischemic events; treatment selection and dosing of warfarin and aspirin; hospital course; and 30-day readmission to the same facility.

Participating hospitals were required to designate a facilitator and to complete a training session for randomization and data collection procedures before patient selection. Medical records were selected using a random numbers table, with the exception of sites that had inherent randomization capability in their medical record system. Chart review was performed on-site by health personnel from the participating institution. A standard data collection form and data dictionary defining each collected element was used. Once data were collected, the site facilitator supervised data entry into the NABOR data entry software. The software was used to remove any patient identifying information, validate the completeness and consistency of entry, and transmit the data via the internet or diskette to the study center for analysis. On receipt by the study center, data were queried for any inconsistencies, and queries were resolved with the site before data entry.

We stratified patients for risk of stroke (2,3). Those with a previous stroke, transient ischemic attack (TIA), or systemic embolus; history of hypertension; left ventricular dysfunction; age >75 years; rheumatic mitral valve disease; or prosthetic heart valve were stratified to high risk. Those with one risk factor, including age 65 to 75 years, diabetes mellitus, or coronary artery disease were stratified to moderate risk, but those with one or more of these risk factors were stratified to high risk. Patents 65 years of age and younger and with no cardiovascular disease were stratified to low risk.

Analysis. To analyze the impact of patient characteristics and stroke risk factors on AF treatment, we used a two-staged analysis strategy. At the univariate stage, we analyzed the following possible predictor variables of AF treatment: age, AF classification (first vs. recurrent event, paroxysmal vs. persistent/permanent event), AF stroke risk category (low, intermediate, high), history of stroke or TIA, and bleeding risk (history of aneurysm, neuropsychologic impairment, past bleeding episode or perceived fall risk) (17). Each possible predictor was examined in relation to warfarin use and no treatment using chi-square methodology. For eight patients with missing documentation of previous stroke, TIA, or systemic embolic event in the medical record, these parameters were assumed to be absent in univariate analysis.

Three logistic regression models were then run with warfarin use as the dichotomous-dependent variable. In the first model, AF risk category, history of stroke, TIA, or systemic embolic event, AF classification, and bleeding risk were entered into the model as independent variables. In the second model, we replaced AF risk category with age. In the third model, we removed all extraneous variables to create a parsimonious model predicting treatment with warfarin. Odds ratios and 95% confidence intervals were calculated. Analyses were conducted using SPSS for Windows version 11.0 (SPSS Inc., Chicago, Illinois) and in a two-tailed fashion, with level of significance set as 0.05.

RESULTS

Patient characteristics. A total of 945 patients were included from 21 academic hospitals, 13 community hospitals, and 4 VA hospitals located in 28 states. Ten were disproportionate share hospitals. The mean age was 71.5 years, of which 43.3% were older than 75 years, and 54.5% were male. Hypertension was the most frequently reported risk factor for stroke (66.9%), in addition to coronary artery

Table 1. Atrial Fibrillation Patient Characteristics

Characteristics	All Patients n = 945
Mean age (yrs)	71.5 ± 13.5
Age range (yrs)	
≤65	270 (28.6)
66–75	256 (27.1)
>75	419 (44.3)
Gender	
Male	515 (54.5)
Female	430 (45.5)
Other clinical characteristics	
Hypertension	632 (66.9)
CAD/atherosclerosis	398 (42.1)
CHF (LV dysfunction)	325 (34.4)
Diabetes	208 (22.0)
Stroke, TIA, or systemic embolus	196 (20.7)
Cigarette smoking	184 (19.5)
AMI history	144 (15.2)
Alcohol abuse	93 (9.8)
DVT or PE history	55 (5.8)
Prosthetic heart valve	33 (3.5)
Rheumatic mitral valve	21 (2.2)
Thyrotoxicosis	8 (0.8)

Values expressed as n (%) or mean ± SD.
AMI = acute myocardial infarction; CAD = coronary artery disease; CHF = congestive heart failure; DVT = deep vein thrombosis; LV = left ventricular; PE = pulmonary embolism; TIA = transient ischemic attack.

disease (42.1%), congestive heart failure (34.4%), and diabetes (22%). One in five (20.7%) reported a previous history of stroke, TIA, or systemic embolic event (Table 1).

Relationship of stroke risk classification to anticoagulant treatment. Of the 945 patients studied, 86.1% were stratified to high risk, 6.5% to moderate risk, and 7.4% to low risk. Figure 1 shows the treatment by risk stratification. In the high- and moderate-risk cohorts, only 54.7% and 54.1% ($p = 0.931$), respectively, were treated with warfarin, whereas 1 in 5 (20.6%) and 3 in 10 (29.5%) ($p = 0.06$), respectively, were untreated, receiving neither warfarin nor aspirin. Patients in VA hospitals more frequently received warfarin in the high-risk cohort (68%) than patients in academic (53%) and community hospitals (53%) ($p = 0.009$). Fifty-two percent of high-risk patients in disproportionate-share hospitals received warfarin, compared with 56% in non–disproportionate-share hospitals ($p = 0.245$). For the entire AF population, warfarin use was similar both during hospitalization (53.5%) and on discharge (54.4%).

Table 2. Atrial Fibrillation—Analysis of Factors in the High-Risk-Not-Receiving-Warfarin Cohort Associated With Perceived or Actual Bleeding Risk

Factors Associated With Perceived or Actual Risk of Bleeding	Frequency n = 814 (%)
Fall risk	339 (41.7)
Neuropsychologic impairment	137 (16.8)
Past bleeding episode	119 (14.6)
Peptic ulcer disease	103 (12.7)
Aneurysm history	42 (5.1)
None of these factors	351 (43.1)

We analyzed the cohort with the highest annual stroke event rate (18), which includes AF patients with a previous history of stroke, TIA, or systemic embolic event. Of the 196 patients in this cohort, only 120 (61.2%) received warfarin. Forty-one (20.9%) received only aspirin, although it is not indicated in guidelines (2,3), and 35 (17.9%) received no treatment.

Further analysis of those in the high-risk cohort (n = 814) was performed to determine possible rationale for not prescribing warfarin. Fall risk was reported in 41.7%, neuropsychological impairment in 16.8%, a past bleeding episode in 14.6%, peptic ulcer disease in 12.7%, and a history of aneurysm in 5.1%. However, none of these factors were reported as present in 43.1% of high-risk patients not receiving warfarin (Table 2).

Relationship of type of atrial fibrillation to anticoagulant treatment. Both classification and type of event were examined to determine their effect on treatment. There was very nearly an even distribution between those classified as paroxysmal (51.4%) and those classified as persistent/permanent (47.9%), although six records could not be

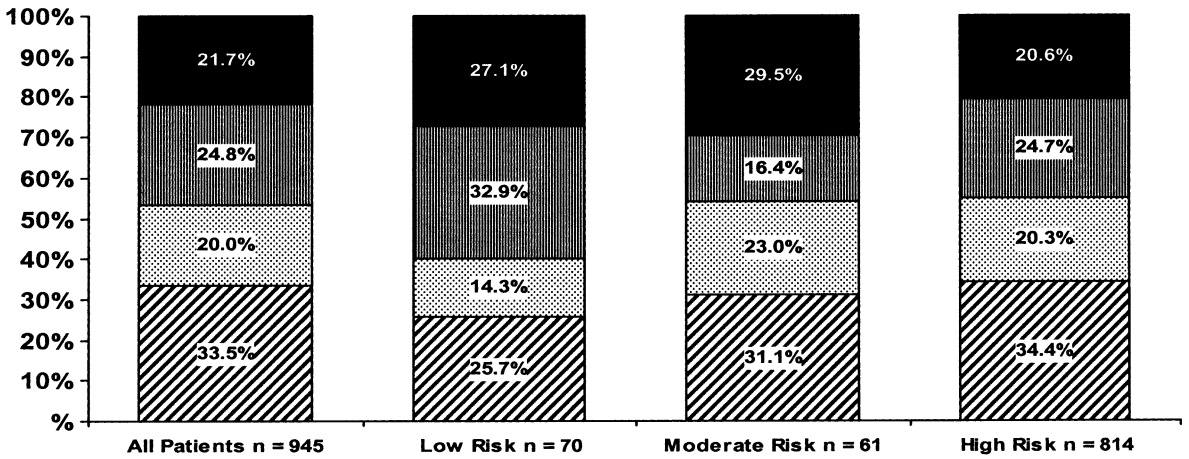

Figure 1. Treatment of atrial fibrillation by risk stratification. **Diagonal-striped boxes** = warfarin; **dotted boxes** = warfarin plus aspirin; **vertical-striped boxes** = aspirin; **black boxes** = no treatment.

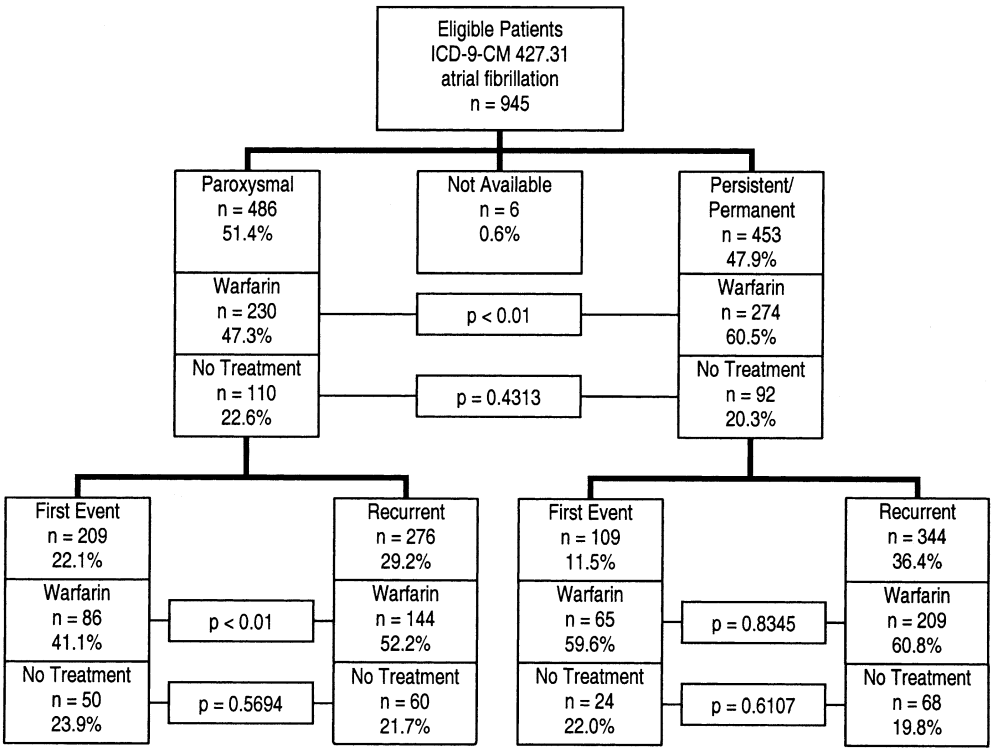

Figure 2. Flow chart of classification, type of event, and treatment for atrial fibrillation.

classified (Fig. 2). Patients with persistent/permanent AF were more often treated with warfarin than those with paroxysmal AF (60.5% vs. 47.3%, $p < 0.01$), despite having a similar proportion of patients with either a high or a moderate risk of stroke (94% vs. 91.2%) ($p = 0.189$). In the paroxysmal cohort, those with a recurrent event were more often treated with warfarin than those with a first event (52.2% vs. 41.1%, $p < 0.01$). However, in the persistent/permanent cohort, there was no significant difference in warfarin use between recurrent and first events (60.8% vs. 59.6%, $p = 0.83$). The same analysis was performed to determine the effect of classification and type of event for those receiving no treatment. No significant differences were found between persistent/permanent and paroxysmal (20.3% vs. 22.6%, $p = 0.51$), nor in the paroxysmal cohort between recurrent and first event (21.7% vs. 23.9%, $p = 0.36$), nor in the persistent/permanent cohort between recurrent and first event (19.8% vs. 22%, $p = 0.61$). Therefore, classification and type of event were not predictors of non-treatment in this univariate analysis.

Relationship of age to anticoagulant treatment and bleeding risk. In determining the effect of age on the risk of bleeding and treatment with warfarin, we analyzed three different age groups, <65, 65 to 75, and >75 years. Using the perceived or actual bleeding risk factors for stroke referenced in Tables 2 and 3, the risk of bleeding increased as age increased from 29% in those <65 years old to 40.5% in those 65 to 75 years, and 63.1% in those >75 years ($p < 0.001$, chi-square test). However, there were no significant differences in the warfarin treatment rates of 52.2%, 57.8%, and 52.1%, respectively ($p = 0.315$) (Fig. 3). There was also no significant difference in the non-treatment rate between age groups (22.6% for <65 years vs. 23.4% for 65 to 75 years vs. 20% for >75 years, $p = 0.33$).

In attempting to find a decision point at which age affected the use of warfarin, we analyzed the differences between those ≥80 years old and those <80 years old. In those <80 years, the warfarin treatment rate was 56.7% versus 46% in those ≥80 years ($p < 0.01$). However, the perceived or actual risk of bleeding was also 1.7 times greater in those ≥80 years old (69.1% vs. 40.5%, $p < 0.001$) (Fig. 3).

We also determined the overall effect of perceived or actual bleeding risk and the individual effect of each bleeding risk factor on use of warfarin in the cohort ≥80 years of age. In this cohort, 64.8% receiving warfarin versus 72.7%

Table 3. Use of Warfarin in Patients ≥80 Years of Age

	Treatment Selection		
	Warfarin n = 128 (%)	**No Warfarin n = 150 (%)**	**p Value**
Perceived or actual risk of bleeding	83 (64.8)	109 (72.7)	0.31
Analysis by risk factor			
Fall risk	64 (50.0)	91 (60.7)	0.15
Neuropsychologic impairment	26 (20.3)	35 (23.3)	0.97
Past bleeding episodes	13 (10.2)	21 (14.0)	0.30
Peptic ulcer disease	9 (7.0)	24 (16.0)	.025
Aneurysm history	7 (5.5)	9 (6.0)	0.58

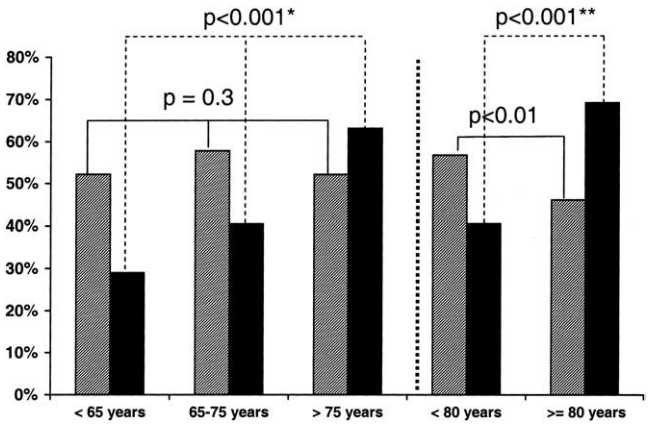

Figure 3. Warfarin use and perceived or actual bleeding risk by age distribution. Bleeding risk includes fall risk, neuropsychological impairment, past bleeding episode, peptic ulcer disease, and aneurysm history. *Chi-square test for trend. **Chi-square. **Ruled boxes** = warfarin use; **black boxes** = perceived or actual bleeding risk.

not receiving warfarin (p = 0.31) had a perceived or actual risk of bleed. The only bleeding risk factor that was a predictor for use of warfarin was peptic ulcer disease, with a reported incidence of 7% in those receiving warfarin versus 16% in those not receiving warfarin (p = 0.025) (Table 3).

Predictors of warfarin use. Three logistic regression models were then run with warfarin use as the dichotomous dependent variable. In the first model, AF stroke risk category; history of stroke, TIA, or systemic embolic event; type of AF; and perceived or actual bleeding risk were entered into the model (Table 4). The AF risk was chosen for incorporation in the model a priori with input from the study committee. Age was not added to the regression model, because age is a primary determinant of AF risk. Including both in the model would introduce colinearity. Persistent/permanent AF; recurrent AF; and history of stroke, TIA, or systemic embolic event each were independent variables associated with increased likelihood of receiving warfarin. Perceived or actual bleeding risk significantly decreased the likelihood of warfarin treatment, but as also indicated in univariate analysis, high-risk stratification was not associated with warfarin treatment.

Table 4. Variables Associated With Treatment With Warfarin

Independent Variables	Odds Ratio	95% Confidence Interval	p Value
Model 1			
Perceived or actual bleeding risk	0.515	(0.38–0.69)	<0.001
Persistent/permanent AF	1.685	(1.28–2.20)	<0.001
Recurrent AF	1.341	(1.01–1.77)	0.042
Stroke/TIA/embolic event	1.482	(1.02–2.15)	0.038
High-risk stratification	1.367	(0.93–2.00)	0.111
Model 2			
Perceived or actual bleeding risk	0.711	(0.53–0.93)	<0.001
Persistent/permanent AF	1.708	(1.30–2.23)	<0.001
Recurrent AF	1.314	(0.99–1.74)	0.058
Stroke/TIA/embolic event	1.559	(1.08–2.25)	0.018
Age >80 yrs	0.678	(0.49–0.92)	0.013
Model 3			
Perceived or actual bleeding risk	0.724	(0.54–0.95)	0.022
Persistent/permanent AF	1.799	(1.37–2.34)	<0.001
Stroke/TIA/embolic event	1.586	(1.09–2.28)	0.014
Age >80 yrs	0.663	(0.48–0.90)	0.008

Abbreviations as in Table 1.

In the second model, we replaced the high stroke risk stratification category with age because univariate analysis suggested that advanced age, despite any other potential association with increased stroke risk, was a negative predictor of warfarin use. Indeed, age >80 years significantly decreased the likelihood of warfarin treatment (odds ratio = 0.678, 95% confidence interval, 0.49 to 0.92, p = 0.013). In this model, the addition of age mitigated a portion of the impact of bleeding risk, indicating potential confounding. However, perceived or actual bleeding risk remained a significant negative predictor of treatment with warfarin (odds ratio, 0.711; 95% confidence interval, 0.53 to 0.093; p < 0.001). Also in this model, recurrent AF was no longer a significant predictor, controlling for the remaining variables in the model. Therefore, in the third and final model, we removed recurrent AF. The remaining variables in the model were each highly associated with warfarin use. Age >80 years and perceived or actual bleeding risk were negative predictors of warfarin use, and persistent/permanent AF and history of stroke, TIA, or systemic embolic event were positive predictors of warfarin use.

DISCUSSION

Numerous, well-done AF trials, published between 1989 and 1996, have shown that warfarin is highly effective in the prevention of stroke and death caused by thromboembolism (6–13). Largely based on these studies, guidelines for the use of warfarin in AF patients at risk of stroke (high- and moderate-risk categories) have been published and are widely accepted (2,3). This study, which was performed in a broad geographic and categorical cross section of U.S. hospitals, showed some aspects of the under-use of warfarin that will help us understand barriers to primary and secondary prevention of stroke. In spite of the risk of stroke being similar for paroxysmal versus persistent/permanent AF, we showed that classification guided the treatment decision for warfarin, and it should not. We showed that age >80 years was a negative predictor of warfarin use in the age group at highest risk of stroke. It was disappointing that stroke risk stratification was not a predictor of warfarin treatment, with the exception of a previous history of stroke, TIA, or systemic embolic event. And even in those with a previous stroke, TIA, or systemic embolic event, the non-treatment rate of 18% was high.

Comparison with warfarin use in other AF studies. The first large study of national patterns of warfarin use in AF was performed by Stafford and Singer (19). Using data from National Ambulatory Medical Care Surveys, their study showed that warfarin use in AF had improved from 7% in 1980 to 1981 to 32% in 1992 to 1993. Likewise, non-

JACC Vol. 46, No. 9, 2005
November 1, 2005:1729–36

Table 5. NABOR Study Results Comparison Published Atrial Fibrillation Anticoagulation Studies

Study Period	Published Studies	Setting	Warfarin Use (%)	Non-Treatment (%)	Study Population
1980–1981	Stafford et al. (19)	Ambulatory	7	90	AF, excluding atrial flutter
1992–1993	Stafford et al. (19)	Ambulatory	32	48	AF, excluding atrial flutter
1990–1993	Antani et al. (21)	Teaching hospitals and ambulatory	23	59	Sustained or intermittent non-rheumatic AF
1992–1994	Albers et al. (20)	Teaching hospitals	41	22	AF, excluding mitral stenosis or heart valves
1993–1994	Whittle et al. (22)	Small rural hospitals	47*	43	AF, Medicare population
1993–1994	Flaker et al. (23)	Rural and urban hospitals	34	45	Non-valvular AF, Medicare population
1993–1995	Gurwitz et al. (34)	Long-term care	32	43	AF, including U.S. and Canada facilities
1994–1995	Munschauer et al. (25)	Hospitals	34†	42	Chronic AF
1994–1996	Bradley et al. (24)	Hospital and ambulatory	51	25	AF, VA population
1996–1997	Go et al. (5)	Large HMO	54‡	Not reported	Nonvalvular AF
1997–1998	McCormick et al. (36)	Longterm care	42	32	AF
1997–2001	Brophy et al. (35)	Ambulatory	35	Not reported	Nonvalvular AF, VA population
1998–2001	Jencks et al. (26)	Hospitals	57	Not reported	AF, Medicare population
2000–2002	NABOR results	Teaching, community, and VA hospitals	54	22	AF

*Warfarin use was 64% in ideal candidates. †Warfarin use was 53% in ideal candidates. ‡Warfarin use was 55% in patients with no contraindications.
AF = atrial fibrillation; HMO = health maintenance organization; NABOR = National Anticoagulation Benchmark and Outcomes Report; VA = Veterans Administration.

treatment declined from 90% to 48%. They showed that a trend of increasing warfarin use coincided with the publication of the Atrial Fibrillation Aspirin and Anticoagulation (AFASAK) study (6), the Stroke Prevention in Atrial Fibrillation (SPAF) study (7–9), the Boston Area Anticoagulation Trial for Atrial Fibrillation (BAATAF) (10), the Canadian Atrial Fibrillation (CAFA) study (11), and the Stroke Prevention in Nonrheumatic Atrial Fibrillation (SPINAF) study (12) between 1989 and 1992. Other studies have been performed in hospitals, long-term care facilities, and health maintenance organizations, showing a range in warfarin use from 32% to 57% and non-treatment from 22% to 59% (Table 5).

Our results show a 54% warfarin use rate, a likely suboptimal treatment rate of 25% with aspirin, and a 22% non-treatment rate in hospitalized patients. It is worth emphasizing that our study represents a broad sample of hospitals across the U.S. and is not limited to academic hospitals (Albers et al. [20]), hospitals within a one-state geography (Antani et al. [21], Whittle et al. [22], Flaker et al. [23]), patients within one hospital/clinic (Bradley et al. [24]), a selected classification of AF (Munschauer et al. [25]), or a Medicare population (Jencks et al. [26], Whittle et al. [22], Flaker et al. [23]). It is important to note from a longitudinal perspective that despite variability in the study populations, warfarin use seems to have reached a plateau at approximately the 55th percentile, since the mid 1990s.

Our population's incidence of major risk factors, including hypertension, coronary artery disease, congestive heart failure, and diabetes mellitus, was 67%, 42%, 34%, and 22%, respectively, compared with Albers et al. (20) with 55%, 30%, 39%, and 22%, respectively, and Go et al. (5) with 51%, 29%, 31%, and 17%. Interestingly, the incidence of hypertension ranged from 32% to 58% in the AFASAK (6), BAATAF (10), CAFA (11), SPINAF (12), and SPAF III (9) trials compared with our 67% incidence. The significance of this comparison is related to the findings of the SPAF III Writing Committee, who reported a 3.6% incidence of primary events in a "low-risk" cohort with hypertension versus a 1.1% much lower incidence of primary events in those without hypertension (27). Our high incidence of hypertension magnifies the need for greater use of anticoagulation in those who are hospitalized.

Effect of bleeding risk on anticoagulation. Those using anticoagulation in AF patients must deal with the dilemma that increasing age increases the risk of both stroke and hemorrhage. This paradox is confounded by other risk factors for bleeding, particularly those for intracranial hemorrhage, such as cerebrovascular disease and hypertension (28), the incidence of which also increases with age. In our cohort, age ≥80 years and the occurrence of overall perceived or actual bleeding risk was not significantly different between those receiving and not receiving oral anticoagulation, with the exception of peptic ulcer disease. However, we wonder whether anticoagulation intensity, which has a strong relationship to both stroke and hemorrhage (28,30), might be a consideration, although it does not seem to be more inherently difficult to maintain therapeutic INRs as patients get older (31). Our findings may suggest that age ≥80 years, alone or in combination with another perceived barrier, other than the commonly professed risk of hemorrhage, is the reason that physicians less frequently prescribe oral anticoagulation to those over 80 years of age.

It was striking that in those high-risk patients not receiving warfarin, 43% had no perceived or actual bleeding

risk factors present. Conversely, fall risk was the most frequently reported bleeding risk factor and was present in 41.7% of the population. If one accepts the conclusion of Man-Son-Hing and Laupacis (17) that the risk of subdural hematoma from falling is remarkably small, then for most of these patients the benefits of anticoagulant therapy outweigh the risks. Therefore, the actual percent of patients not receiving warfarin who were appropriate candidates for anticoagulation might more realistically approximate 62%, which represents those with no perceived or actual bleeding risk other than the risk of fall.

Predictors of warfarin use. This study points to an additional factor, aside from the commonly reported factors of previous stroke, bleeding history, or increasing age, as being predictive of warfarin use. A classification of persistent/permanent AF was associated with a 1.8-fold increase in the odds of receiving warfarin. Others have not analyzed this effect, perhaps because analyses of trial data have indicated that the rate of stroke is similar for both paroxysmal and chronic atrial fibrillation (32,33).

Go et al. (5), Antani et al. (21), Gurwitz et al. (34), and Brophy et al. (35) each analyzed positive and negative predictors for warfarin use in their respective studies of AF. They also noted the relationship of such factors as previous stroke, advanced age, and risk of hemorrhage predicting the use or non-use of warfarin. To our knowledge, we are the first to analyze and report persistent/permanent AF as a predictor of warfarin use.

In an era of international guidelines, we would expect that risk stratification for a high risk of stroke would have been predictive of warfarin use. However, the slight trend observed was not statistically significant. Likewise, McCormick et al. (36) in a study of long-term care patients showed that the odds of receiving warfarin increased with increasing number of stroke risk factors present, although this did also not reach statistical significance.

Study limitations. Composition of the participating hospitals was a potential source of bias, with respect to our findings being representative of U.S. hospitals. Academic hospitals contributed 55% of the study population, whereas community and VA hospitals contributed 34% and 11%, respectively. In addition, we identified patients only by ICD-9-CM code, and did not require confirmation of a diagnosis by an interpretable electrocardiogram. Others have noted the potential for misdiagnosis because of incorrect computerized interpretation of electrocardiogram, combined with failure of the ordering physician to correct the erroneous interpretation (37). We did not collect patient preference data regarding the use of warfarin from notations that might have been made in the medical record. We also did not exclude patients who had had open-heart surgery, a group in which AF is often transient. Another limitation is that our data lack information on use of warfarin after hospital discharge, because many chronic medications are not necessarily initiated in the hospital setting. However, we believe that when indicated, it is usual practice to initiate warfarin therapy at the first opportunity. Thus, we would have expected that in most instances, warfarin therapy would have been initiated in the hospital, and continued on an out-patient basis, making indicated dose adjustments until a stable INR in the therapeutic range was achieved. Also, the data were presumably from 2002, and in that sense, not totally contemporary. However, importantly, the American College of Cardiology/American Heart Association/European Society of Cardiology guidelines (3) were published in September 2001, making these data uniquely timely.

Conclusions. Most hospitalized AF patients have a high risk of stroke, particularly cardioembolic stroke. Data show that warfarin reduces the risk of cardioembolic stroke. However, warfarin is only used between 50% and 60% of the time in those AF patients with the greatest stroke risk. Contraindications to warfarin do not account for this level of under-use. Despite landmark clinical trials showing the benefits of warfarin to prevent stroke, the level of non-treatment and suboptimal treatment observed reflects either the real-world limitations of warfarin, disregard for risk-guided treatment, or both.

Reprint requests and correspondence: Dr. Albert L. Waldo, University Hospitals of Cleveland, Division of Cardiology, 11100 Euclid Avenue, Cleveland, Ohio 44106-5038. E-mail: albert.waldo@case.edu.

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APPENDIX

For a list of the institutions involved in this study, please see the online version of this article.

Hospitalized Patients With Atrial Fibrillation and a High Risk of Stroke Are Not Being Provided With Adequate Anticoagulation

Albert L. Waldo, Richard C. Becker, Victor F. Tapson, Kevin J. Colgan, for the NABOR Steering Committee

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