Heart Rhythm Disorders

Trends in Anticoagulation for Atrial Fibrillation in the U.S.

An Analysis of the National Ambulatory Medical Care Survey Database

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Objectives	The purpose of this study was to track trends in the use of anticoagulation for atrial fibrillation (AF) over the past decade and identify predictors of use.
Background	Atrial fibrillation is common and associated with significant morbidity. Previous studies suggest underuse of anticoagulant therapy in patients with AF.
Methods	The National Ambulatory Medical Care Survey database was queried for all patient visits with a diagnosis of AF between 1994 and 2003. Other diagnoses, other medications, and demographic, visit, geographic, and provider characteristics were compared with the prescription of anticoagulation in predefined age and risk groups.
Results	The prevalence of the diagnosis of AF and anticoagulation for AF has increased over the last decade. Increased age and use of rate control agents is associated with the use of anticoagulation. There is a trend toward less anticoagulation when a rhythm control agent is used instead of a rate control agent. Anticoagulation might be overused in a group of low-risk patients.
Conclusions	From 1995 through 2002, an increase has occurred in anticoagulation for AF, especially in those at highest risk for thromboembolic phenomena. A substantial number of patients at risk for thromboembolic events are not anticoagulated, and further studies are needed to determine how many of these patients are candidates for anticoagulation. Anticoagulation use has increased in nontargeted, low-risk groups in whom antiplatelet agents are appropriate. Use of a rhythm control agent might be associated with less use of anticoagulation. (J Am Coll Cardiol 2007;49:1561–5) © 2007 by the American College of Cardiology Foundation

Atrial fibrillation (AF) is a common supraventricular arrhythmia that occurs in approximately 2.4 million inhabitants of the U.S. Because its incidence increases with age, the population over the age of 65 bears most of the burden of AF (1). Much of this burden is a result of the increased risk of embolic stroke associated with the diagnosis. Individuals with nonvalvular AF have a 5% annual risk of ischemic stroke, a risk level that is 2 to 5 times greater than that of age-matched control subjects (2).

Anticoagulation with warfarin attenuates the ischemic stroke risk associated with AF; unfortunately, anticoagulation itself carries a significant risk of bleeding complications (3,4). In an effort to help clinicians balance this risk-benefit equation, several groups have published evidence-based guidelines that delineate higher-risk patient populations for whom anticoagulation is recommended and lower-risk populations for whom it might not be necessary (3,5–7). Several previous studies have shown that, despite these guidelines, anticoagulation might be underused in some high-risk populations with AF (8–13).

The present study was thus undertaken with 4 goals in mind. First, we wanted to describe the AF patient population between 1994 and 2003. Second, in view of ongoing widespread emphasis regarding the need for anticoagulation for high-risk individuals, we tested the hypothesis that the rate of appropriate anticoagulation would be increasing over time. Third, a recent meta-analysis suggested that increased morbidity in patients taking antiarrhythmic agents might be partially due to non-anticoagulation of this group (14). Therefore, we hypothesized that patients receiving antiarrhythmic therapy would be treated with anticoagulation less often than patients receiving nodal-blockade therapies. Fourth, although there is information available on the patterns of anticoagulation of patients with AF at increased risk for thromboembolic events, there is virtually no information on the use of anticoagulation in patients with AF at lower risk for thromboembolism. We tested the hypothesis that such low-risk individuals would, as suggested by current guidelines, not be treated with anticoagulation.

Methods

The National Ambulatory Medical Care Survey (NAMCS) database is composed of the records of the responses of a nationally representative, non-federally employed group of ambulatory physicians to a standardized survey instrument. Patient visits to selected practices within a geographically defined primary sampling unit are entered by the providing physician into the survey form. The form includes fields for demographic data, up to 3 diagnoses, and up to 8 medications. Keying and coding of survey responses with International Classification of Diseases, 9th Revision (ICD-9) codes and National Drug Code numbers are performed by a central agency with internal quality control procedures and an error rate of 0% to 1% (15).

We combined the 1994 through 2003 NAMCS data sets in order to produce reliable national estimates regarding the use patterns of anticoagulant therapy among patients diagnosed with AF. The NAMCS estimates are considered reliable by the National Center of Health Statistics (NCHS) standards if the sample of patient visits/unit cell is >30 and the relative standard error (RSE) (standard error/estimate) is <0.30. The NAMCS patients 18 years of age or older with a diagnosis of AF (ICD-9 = 427.31) in any of the 3 NAMCS diagnosis fields (diag1 to diag3) were identified for the analysis. In addition, with the NAMCS diagnosis fields (diag1 to diag3) and medication fields (med1 to med8; gen1 to gen8), each patient's significant comorbidities (diabetes, hypertension, congestive heart failure, and cerebrovascular accident) and usage of anticoagulant therapy (warfarin), rate control agents (a composite of beta-blocker therapy, nondihydropyridine calcium channel blocker therapy, and digitalis compounds), and antiarrhythmic agents (amiodarone, sotalol, propafenone, procainamide, quinidine, flecainide, disopyramide, moricizine, and dofetilide) were also identified. General demographic information (gender, race, metropolitan statistical area, region, physician specialty, age category, and insurance type) were used to describe the entire population with AF. The same analysis was performed in the 18 to 64 and 65 years of age or older populations.

Univariate and comparison analyses. Patients with AF receiving anticoagulant medications were categorized as receiving anticoagulant therapy if the patient received at most 1 prescription of warfarin or coumadin during the visit. Otherwise, the patient was categorized as not receiving anticoagulant medications. Medication and comorbidities were categorized similarly with the diagnosis and medication fields. Chi-square tests were then performed to determine general univariate associations among all patients with AF receiving anticoagulation medications and those not receiving anticoagulation medications and patients' gender,

race, metropolitan statistical area, region, physician specialty, age category, insurance type, comorbidity, and medication usage. Because increasing age is considered a risk

Table 1 — **Relative Frequency of Anticoagulation by Selected Visit Characteristics**

Visit Characteristic	n	Anticoagulation With Warfarin (%)		
		Yes	No	p Value
Total patients with atrial fibrillation	40,506,313	45.66	54.34	
Age category, yrs				
18–59	4,545,314	34.33	65.67	0.0192*
60–75	14,794,448	45.00	55.00	
76+	21,166,551	48.55	51.45	
Patient's gender				
Female	19,794,635	42.53	57.47	0.0890
Male	20,711,678	48.65	51.35	
Patient's race				
White/non-Hispanic	36,672,549	46.37	53.63	0.2601
Other	3,833,764	38.81	61.19	
Location				
Metropolitan	31,304,831	45.58	54.42	0.9399
Non-metropolitan	9,201,482	45.94	54.06	
Northeast	9,557,308	51.53	48.47	0.1718
Midwest	9,916,927	44.10	55.90	
South	12,522,707	40.07	59.93	
West	8,509,371	49.11	50.89	
Provider				
Cardiologist	13,467,795	46.54	53.46	0.7009
Other	27,038,518	45.22	54.78	
Patient's insurance				
Private	8,259,928	38.37	61.63	0.0188
Public	29,451,917	48.63	51.37	
Other	2,794,468	35.86	64.14	
Other diagnosis				
Diabetes				
Yes	2,624,169	37.25	62.75	0.2142
No	37,882,144	46.24	53.76	
Congestive heart failure				
Yes	5,963,331	50.17	49.83	0.3003
No	34,542,982	44.88	55.12	
Hypertension				
Yes	8,366,979	52.72	47.28	0.0647
No	32,139,334	43.82	56.18	
Ischemic cerebrovascular event				
Yes†	1,236,976	70.42	29.58	0.0325
No	39,269,337	44.88	55.12	
Any comorbidity				
Yes	16,162,670	50.83	49.17	0.0276
No	24,343,643	42.23	57.77	
Therapy with				
Any rate agent				
Yes	21,733,522	56.29	43.71	<0.001*
No	18,772,791	33.35	66.65	
Any rhythm agent				
Yes	5,018,028	44.12	55.88	0.6875
No	35,488,285	45.87	54.13	

*p < 0.01. †Unreliable estimate by National Center for Health Statistics standards. Results are preliminary.
n = weighted number of patient visits with a diagnosis of atrial fibrillation.

factor for thromboembolism with AF, similar chi-square analyses were performed among patients with AF 18 to 64 years of age without known congestive heart failure, previous cerebrovascular event, hypertension, or diabetes mellitus. Because sample sizes for this analysis were small, reliability of the estimates could not be made; therefore, the results of this analysis should be considered preliminary.

Owing to multiple testing, statistical significant associations are determined at the alpha level of 0.01.

To compare the use of anticoagulant medications among patients with AF receiving antiarrhythmic therapies with those receiving rate control therapies, a 2-sample *t* test was performed. For this analysis, patients with AF who received both rate and rhythm control medications were eliminated from the analysis.

Time trend analysis. Time trend analyses were performed to determine whether the odds of receiving anticoagulant medication increased each year among all AF patients. Simple logistic regression analyses were performed for anticoagulation usage (yes, no) adjusted for survey year as a continuous variable. To determine whether the odds of anticoagulation usage are increasing differently among AF patients by age, similar stratified simple logistic analyses were also performed among patients 18 to 59 years, 60 to 75 years, and 76 years or older segregated by the presence or absence of a comorbid condition known to be associated with increased thromboembolic risk (known congestive heart failure, previous cerebrovascular event, hypertension, or diabetes mellitus). In addition, descriptive statistics (percent, weighted estimates) for each age strata were also included in terms of 3 equal time periods (1995 to 1997, 1998 to 2000, and 2001 to 2003).

Because NAMCS patient visits are sampled with a multistage probability sample design, all analyses were performed with SUDAAN 9.1 software (Research Triangle Institute, Research Triangle Park, North Carolina) and the NAMCS patient weight. All estimates were tested for reliability by NCHS standards. Unreliable estimates are noted in the text and tables.

Results

During the 1994 to 2003 time period, approximately 40.5 million AF patient visits occurred. Of these patients, 18.0 million (45.6%) received anticoagulant therapy. Among all patients with AF, age and use of "rate control" agents were associated with receiving anticoagulant therapy. A higher proportion of patients 60 years of age or older received anticoagulant therapy compared with patients 18 to 59 years of age. A higher percentage of patients with AF receiving "rate control" agents received anticoagulant therapies. Patients' gender, race, metropolitan status, geographical area, type of treating physician, insurance type, individual comorbities, and use of a rhythm agent were not significantly associated with anticoagulant use (Table 1).

The frequency with which AF was listed as a diagnosis increased over the period between 1994 and 1997 and 2001 to 2003 (Table 2). The overall frequency of anticoagulation also increased from 40.3% of all patients with AF between 1994 and 1997 to 49.1% during the 2001 to 2003 time period. The relative frequency of anticoagulation—comparing the same time periods—increased by 80% in the 18- to 59-year-old population, decreased by 8% in the 60- to 75-year-old population, and increased by 45% in the 76 and older population. Logistic regression analyses deter-

Table 2	Percentage of Patients With Atrial Fibrillation Taking Anticoagulation by Time Period and Age Group								
	1995–1997		**1998–2000**		**2000–2002**				
	Total	**% Anticoagulated**	**Total**	**% Anticoagulated**	**Total**	**% Anticoagulated**	**OR**	**95% CI**	**p Value**
Ages 18–59 yrs									
Total	1,073,378	24.08%*	1,871,404	32.44%	1,600,532	43.40%	1.16	(1.00–1.35)	0.0436†
With comorbidity	291,620†	28.40%*	700,351*	52.18*	449,053†	58.27%*			
Without comorbidity	781,758	22.46%*	1,171,053	20.64*	1,151,479	37.60%*			
Ages 60–75 yrs									
Total	4,117,539	49.22%	4,476,365	40.77%	6,200,544	45.25%	1.00	(0.91–1.09)	0.9247
With comorbidity	1,548,309	43.31%	1,730,889	54.96%	1,993,137	46.18%			
Without comorbidity	2,569,230	52.78%	2,745,476	31.82%	4,207,407	44.81%			
Ages 76+ yrs									
Total	4,627,721	36.02%	6,324,152	51.61%	10,214,678	52.34%	1.11	(1.02–1.19)	0.0097†
With comorbidity	2,051,851	37.98%	2,509,379	51.97%	4,888,081	58.90%			
Without comorbidity	2,575,870	34.45%	3,814,773	51.37%	5,326,597	46.31%			
All patients									
Total	9,818,638	40.25%	12,671,921	44.95%	18,015,754	49.10%	1.07	(1.01–1.13)	0.0181†
With comorbidity	3,891,780	39.38%	4,940,619	53.05%	7,330,271	55.40%			
Without comorbidity	5,926,858	40.82%	7,731,302	39.77%	10,685,483	44.78%			

The odds ratio (OR) represents anticoagulant usage adjusted for survey years as a continuous variable. *Unreliable estimates by National Center for Health Statistics standards. Results are preliminary. †p < 0.05.

CI = confidence interval; Total = weighted number of patient visits with a diagnosis of atrial fibrillation.

mined an overall yearly increase of 7% in the odds of receiving anticoagulant therapy among all patients with AF during this time period. As noted in Table 2, the use of anticoagulation over time was somewhat selective inasmuch as it was greater in patients with comorbid conditions associated with thromboembolic phenomena than in those without these conditions.

We next examined the frequency of anticoagulation use in patients treated exclusively with "rate control" agents (beta-blocker therapy, calcium channel blocker therapy, and digoxin) compared with patients treated exclusively with "rhythm control" agents (any antiarrhythmic). There was a trend toward the use of anticoagulant therapy more commonly in patients taking rate control agents than in those taking rhythm control agents (58.4% vs. 47.1%, respectively, p = 0.0596).

Finally, we examined the frequency of anticoagulation in patients with AF whom most practice guidelines would classify as at relatively low risk for a thromboembolic event: individuals under 65 years of age without known congestive heart failure, previous cerebrovascular event, hypertension, or diabetes mellitus. Interestingly, 30.1% of this low-risk group of 5,037,812 patient visits was anticoagulated. There were no demographic, geographic, or therapeutic characteristics that were associated with the use of anticoagulant therapy in this group. Interestingly, having a cardiologist as a provider was associated with a more than 2-fold chance of receiving anticoagulant therapy in these low-risk patients; however, results of this analysis are considered preliminary, because estimates are unreliable by NCHS standards owing to relatively small sample sizes (Table 3).

Discussion

Our analysis of the NAMCS database provides several interesting insights into the use of anticoagulation for AF in contemporary general medical practice in the U.S. First, the frequency of diagnosis of AF continues to increase. This finding correlates well with other studies that have documented a similar rise (1).

Second, adherence with guidelines for anticoagulation of patients at relatively high risk for thromboembolic phenomena seems to be improving. Our univariate analyses suggests that there are various factors, such as insurance status, comorbid conditions (congestive heart failure, hypertension, and diabetes mellitus), and the use of a "rate control" agent, that are associated with use of anticoagulation. It is noteworthy, however, that the factors associated with "appropriate" use of anticoagulation in patients with AF might be complex. The factors we identified differed from those described previously by Stafford et al. (16) in which a history of stroke, residence outside of the South, age <80, and treatment by a cardiologist or internist were significantly correlated with "appropriate" use of anticoagulation. Also, many patients with AF at risk for thromboembolic events that qualify for anticoagulant therapy are not receiving it.

Table 3	Relative Frequency of Anticoagulation in Patients Age 18 to 64 Yrs by Selected Visit Characteristics			
	Anticoagulation With Warfarin (%)			
Visit Characteristic	**n**	**Yes**	**No**	**p Value**
Patient's gender				
Female*	1,303,849	30.86	69.14	0.8915
Male	3,733,963	29.80	70.20	
Patient's race				
White/non-Hispanic	4,442,923	31.15	68.85	0.3734
Other*	594,889	22.09	77.91	
Location				
Metropolitan	4,059,233	32.57	67.43	0.2237
Non-metropolitan*	978,579	19.75	80.25	
Northeast*	1,129,095	38.34	61.66	0.6347
Midwest*	1,381,887	27.33	72.67	
South*	1,709,157	25.39	74.61	
West*	817,673	33.10	66.90	
Provider				
Cardiologist	2,396,086	44.82	55.18	0.0002†
Other*	2,641,726	16.70	83.30	
Patient's insurance				
Private	3,158,519	33.93	66.07	0.0724
Public*	910,087	34.38	65.62	
Other*	969,206	13.49	86.51	
Therapy with				
Any rate agent				
Yes	2,407,791	35.77	64.23	0.1285
No	2,630,021	24.86	75.14	
Any rhythm agent				
Yes*	1,054,709	49.63	50.37	0.0150
No	3,983,103	24.90	75.10	

*Unreliable estimate by National Center for Health Statistics standards. Results are preliminary. †p < 0.01.

n = weighted number of patient visits with a diagnosis of atrial fibrillation.

However, a significant proportion of these patients might not be reasonably good candidates for anticoagulation, and estimates as to the "target" goal for anticoagulation of selected high-risk populations with AF remains to be better defined. Our results might therefore underestimate the appropriate use of anticoagulation in patients with AF.

Third, it seems that recent increases in the use of anticoagulant therapy have occurred primarily in the youngest (age 18 to 59 years) and oldest (age 76 years and older) with comorbid conditions predisposing to thromboembolic events. The trend for increasing anticoagulation in the oldest populations with comorbid conditions is encouraging, because previous research suggests possible underuse of anticoagulation in this population (10,16).

Fourth, in patients receiving antiarrhythmic therapy, there is a suggestion that anticoagulation is particularly underused. Although this trend did not quite reach statistical significance, it is of particular concern, given recent data that patients taking antiarrhythmic therapy continue to have a significant risk of embolic events (17). The attitude that Brodsky et al. (18) demonstrated a decade ago—that patients with paroxysmal AF may be treated with aspirin alone—likely persists today. It seems likely that physicians

believe, despite evidence to the contrary, that antiarrhythmic therapy effectively prevents recurrent AF in all patients and thus obviates the need for anticoagulation (19).

Finally, there might be potential for overuse of anticoagulation in younger patients. Although the guidelines vary somewhat in age cutoffs and risk factors, it is clear that many of the patients under the age of 65 with no clear risk factors that we identified could, by current guidelines, have been treated with aspirin alone (5,6). The use of anticoagulation potentially exposes this population to an unnecessary risk of hemorrhagic complications. The phenomenon of "spread" of a therapy from targeted populations to other populations for whom the therapy is not indicated or even contraindicated has been observed previously in patients with heart failure (20). It should be noted, however, that our studies do not address the issue of anticoagulation occurring in the context of either pharmacologic or electrical cardioversion of AF. It is possible that younger, lower-risk individuals with AF either seek or are referred to cardiologists and are anticoagulated in association with attempts at cardioversion. Clearly, further studies are indicated as to the reasons for anticoagulant use in "lower-risk" individuals with AF.

Conclusions

The use of anticoagulation for AF has slowly increased in the last decade. This increase in use seems to have occurred at both ends of the age spectrum. Although this increased use is encouraging, there are 2 important caveats. First, many patients are still not receiving anticoagulation. Patients receiving therapy meant to maintain sinus rhythm might be at a higher risk for underuse of anticoagulation than those taking "rate control" therapies. Second, the increase in use of anticoagulation seems to have been particularly notable among patients who might not benefit from this therapy.

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