Quality of Anticoagulation Control Among Patients With Atrial Fibrillation

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Objectives: To assess the level of anticoagulation control achieved in patients with atrial fibrillation (AF) receiving routine medical care within a large managed care organization and to explore patient factors that influence control.

Study Design: Retrospective cross-sectional study of all patients with AF treated in Clalit Health Services (CHS) community clinics in central Israel between November 1, 2006, to October 31, 2007.

Methods: Using the CHS computerized database, we identified 906 patients with a diagnosis of AF who were treated with warfarin for at least 6 months. Data included patient demographics, comorbidities, and international normalized ratio (INR) values as well as managing physician certification. Anticoagulation control was assessed by measurement of time within therapeutic range (TTR) (INR 2-3). Univariate and multivariate analyses were performed to explore the association of patient variables with anticoagulation control.

Results: Roughly two-thirds of patients had poor anticoagulation control, as evidenced by TTR of <60%; the mean TTR was 48.6%. Poor control was significantly associated with female sex, advancing age, and comorbid conditions. Heart failure and having a non–board-certified physician were found to be independent predictors of poor control (odds ratio [OR] = 1.63; 95% confidence interval [CI] = 1.20-2.22; and OR = 1.41; 95% CI, 1.05-1.88, respectively).

Conclusions: Quality of anticoagulation in patients with AF receiving routine medical care was suboptimal, with nearly half the time spent outside the therapeutic range. Ways to improve anticoagulation control among patients with AF should be sought.

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Atrial fibrillation (AF), the most common cardiac rhythm disorder, heightens the risk for ischemic stroke 4- to 5-fold.[1] The use of oral anticoagulants such as warfarin has been shown in clinical trials to reduce the risk of stroke by 64%; thus, warfarin therapy is widely accepted in patients with AF and is advocated by the American College of Chest Physicians.[2,3]

In order to achieve maximal protection against stroke and to minimize bleeding complications, warfarin therapy must be tightly controlled and maintained within a narrow therapeutic index of international normalized ratio (INR) values between 2 and 3. This task is by no means trivial as each INR determination, which requires a venipuncture, needs to be promptly addressed by the managing physician. Moreover, INR levels are influenced by an array of factors including patient age, comorbidities, concurrent medications, genetic makeup, and diet.[4,5] As a result, oral anticoagulant therapy necessitates regular and diligent monitoring, which can be toilsome for patients and physicians alike.

Although not easily achieved, high anticoagulation control, expressed as the time spent within the therapeutic range (TTR), has a paramount affect on patient outcomes, reducing stroke events and mortality rates.[6,7] Moreover, it is estimated that optimal anticoagulation could prevent 28,000 cases of stroke in the United States annually, leading to a $2.5 billion cost reduction.[8]

Even though the literature acknowledged the superior outcomes of anticoagulation clinics over routine medical care in terms of anticoagulation control, anticoagulation management often is in the primary care physician's domain.[9,10] Nevertheless, there is a relative paucity of data concerning the quality of anticoagulation achieved in routine medical care, although it is assumed to be the most prevalent form of anticoagulation care in the United States.[11] Moreover, studies that addressed anticoagulation care in the community were seldom population based; thus, they had selection bias that limited their generalization to other populations.[12-15] Also, previous studies looking at anticoagulation control in the managed care setting had a heterogeneous patient population (ie, some patients received care in the community, while others were treated in anticoagulation clinics), which interfered with evaluation of the anticoagulation control achieved in routine medical care.[16]

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In this article we describe the quality of anticoagulation control achieved in patients with AF receiving routine medical care within a large managed care organization (MCO) in Israel. The purpose of this study was to assess the quality of anticoagulation control (expressed as TTR) and to explore patient-level factors that may have affected it.

Take-Away Points

Because adequate anticoagulation control in patients with atrial fibrillation is of medical and economical importance, it should be optimized.

- In the present study, patients with atrial fibrillation receiving routine medical care within a large managed care organization had suboptimal anticoagulation control.
- Patients receiving oral anticoagulants spent less than half the time within the recommended therapeutic range, and therefore were at heightened risk for medical complications, mainly stroke.
- Patients with comorbidities were more likely to have poor anticoagulation control.

METHODS

This study was carried out in the central district of Clalit Health Services (CHS), Israel's largest government-funded MCO. The central district of CHS provides medical care to approximately 500,000 patients residing in central Israel, a largely urban setting. All patients had full medical coverage by CHS inclusive of pharmacy benefits for prescription medication as granted to all Israeli citizens by order of the National Health Insurance Act.

Following approval of the CHS local institutional review board, we conducted a retrospective study from November 1, 2006, to October 31, 2007, using the CHS computerized database to identify all patients with a diagnosis of AF who were treated with warfarin for at least 6 months. Patients were excluded if they fulfilled any 1 of the following criteria: (1) were younger than 18 or older than 85 years; (2) were elderly and lived permanently in a nursing home; (3) had an active malignancy; (4) had prosthetic heart valves; (5) were bedridden; (6) were prescribed antipsychotic medication; or (7) had fewer than 5 INR determinations during the study period. All records retrieved from the database were audited manually by study staff for concordance with the above-mentioned criteria.

A total of 906 patients met the study criteria and were included in the analysis. Each patient was managed by his/her personal physician during the study period. Overall, care was delivered by 124 primary care physicians in CHS community clinics. The computerized database provided demographics (age, sex) and medical diagnoses. In addition, the number and value of INR determinations for each patient were also extracted. Data on physicians' board certification were retrieved from administrative records.

Anticoagulation control was assessed by measurement of time spent within the TTR (ie, time in which patient INR values were between 2 and 3). The therapeutic range was calculated with computer software that utilized a linear interpolation model, as described by Rosendaal et al.[17] First, the TTR was determined for each patient. Later, stratification of patients according to TTR level was carried out as follows: a TTR level <60% was considered to represent poor anticoagulation control, a TTR level between 60% and 75% was considered to represent good anticoagulation control, and a TTR level >75% was considered to represent excellent anticoagulation control. This stratification allowed characterization of patient subsets associated with the different control levels.

All statistical analyses were performed using SPSS, version 15.0 (SPSS Inc, Chicago, IL). Each potential predictor of poor control was first assessed in univariate models (χ^2 test for categorical variables and analysis of variance for continuous variables). Significant univariate predictors were subsequently assessed in the multivariate logistic regression model to determine their independent effect, expressed as odds ratio (OR) and 95% confidence interval (CI). $P < .05$ was considered significant.

RESULTS

A total of 906 patients with AF who were treated with warfarin for at least 6 months were identified through the computerized database. **Table 1** presents patient demographics and clinical characteristics. The mean age was 71.7 years; 51.9% were female and more than 90% of patients had at least 1 risk factor for ischemic stroke (age ≥75 years, diabetes mellitus, hypertension, heart failure, or prior stroke). Patients were receiving routine medical care delivered mainly by non–board-certified physicians and by board-certified family physicians (48.6% and 37.1%, respectively).

Patients had 769 patient-years of follow-up (mean 310.6 days per patient), during which 14,935 INR determinations were performed. Due to the interpolation method, 137 patient-years could not be evaluated for TTR since INR determinations were performed more than 30 days apart.[17] Patients had a mean of 16.5 INR determinations during the study period (range 5-75) and spent 48.6% of the time within the therapeutic range of 2 to 3, 32% of the time under the therapeutic range, and 19.3% of time above the therapeutic range (**Table 2**).

When patients were stratified according to anticoagulation control levels (TTR <60%, TTR 60%-75%, TTR

Table 1. Demographic and Clinical Characteristics of Patients

Characteristic	No. (%) of Patients (N = 906)
Mean (SD) age, y	71.7 (9.0)
Female	470 (51.9)
Coronary artery disease	526 (58.1)
Stroke risk factor	
Age ≥75 y	406 (44.8)
Diabetes mellitus	260 (28.7)
Hypertension	734 (81.0)
Heart failure	372 (41.0)
Prior stroke	166 (18.3)
Managing physician certification[a]	
Not board certified	440 (48.6)
Family medicine	336 (37.1)
Internal medicine	59 (6.5)
Geriatrics	36 (4.0)
Other	2 (0.2)

[a]For 33 patients, the physician specialty was unknown.

>75%), more than two-thirds of them had poor anticoagulation control (Table 3). Only 11.9% had excellent anticoagulation control, and 20.6% had good anticoagulation control. Compared with the group that had poor anticoagulation control, the group that had excellent anticoagulation control had younger patients and fewer females (P = .006 and P = .02, respectively). Additionally, poor anticoagulation control was associated with more frequent INR testing than excellent control. It was also noticeable that the excellent-control group was less burdened by the comorbidities of diabetes, heart failure, and stroke (P = .003, P <.001, and P = .001, respectively).

Patients with poor anticoagulation control were seen more often by non–board-certified physicians than patients with excellent anticoagulation control (53% poor control vs 40% excellent control, P = .018). An opposite trend appeared among board-certified family physicians, but it did not reach significance (36% poor control vs 45% excellent control, P = .096) (Table 3).

In order to evaluate the independent effect of each variable as a predictor of poor anticoagulation control, we performed a multivariate logistic regression (Table 4). We identified 2 significant predictors of poor anticoagulation control: having a non–board-certified physician and heart failure (OR = 1.41; 95% CI, 1.05-1.88; and OR = 1.63; 95% CI, 1.20-2.22, respectively).

DISCUSSION

In our study, patients with AF receiving routine medical care within a large MCO had suboptimal anticoagulation control with a mean TTR of 48.6%. Additionally, poor anticoagulation control was associated with comorbidities and having a non–board-certified physician. Since a close correlate between anticoagulation control and clinical outcomes (ie, stroke, bleeding events) exists, suboptimal control has profound medical and economic implications.[6,7]

Our results are fairly consistent with those of previous studies where anticoagulation control in routine medical care was assessed, as evident in a recent meta-analysis by Baker et al that found community-based AF anticoagulation control to be 51% (95% CI, 47%-55%) and anticoagulation clinic control to be 63% (95% CI, 58%-68%).[10] This explains to some extent the lower efficacy of oral anticoagulants in stroke prevention in the community setting.[18,19] Different patient characteristics are a possible reason for discrepant control levels in clinical trials/anticoagulation clinics compared with community clinics. This may be especially true among populations burdened by comorbidities such as ours. Indeed, our patient population had a heightened prevalence of comorbidities (diabetes 28.7%, heart failure 41.0%, and stroke 18.3%). All of these comorbidities were significantly associated with poor TTR control (P = .003, P <.001, and P = .001, respectively). It is noteworthy that heart failure has been the only medical comorbidity found to be an independent predictor of poor TTR control (OR = 1.63; 95% CI, 1.20-2.22). An explanatory mechanism is the possible interaction between warfarin and multiple drugs administered to heart failure patients.[5]

Additionally, our data imply that older age is more prevalent in the poor control group (P = .006), unlike results reported by Rose et al, which did not show an age difference among anticoagulation control groups.[12] It is plausible that this finding is a surrogate for the higher burden of comorbidities associated with increasing age. Also, our study found a greater proportion of women in the poorly controlled group (P = .021), consistent with the results of the aforementioned study. Further research is needed to explore sex-related differences in anticoagulation control, especially in light of the heightened risk for stroke among women with AF.[20]

As mentioned above, anticoagulation control achieved in anticoagulation clinics and in clinical trials is superior to that achieved in community clinics.[9,13-15,21] Nevertheless, control levels attained in different community settings vary widely. While some studies report high-quality anticoagulation control with TTR levels above 65%,[22-24] others demonstrate poor anti-

coagulation control with TTR levels below 50%.[14,15,25] Aside from patient selection bias that could explain the above-mentioned discrepancy, our study suggests that physicians' certification also had an effect on anticoagulation control even within the same setting. Hence, more patients managed by non–board-certified physicians as opposed to patients seen by board-certified family physicians were found in the poor control group. Indeed, having a non–board-certified physician was an independent predictor of poor anticoagulation control (OR = 1.41; 95% CI, 1.05-1.88).

Table 2. Anticoagulation Surveillance and Control Among Patients

Parameter	Value
INR testing and surveillance, mean (SD), No.	
Days of surveillance	310.6 (57.1)
INR determinations	16.5 (10.5)
Time distribution regarding therapeutic range, % (SD)	
Time spent under therapeutic range	32.0 (25.5)
Time spent within therapeutic range	48.6 (23.1)
Time spent above therapeutic range	19.3 (18.2)

INR indicates international normalized ratio.

This finding may be related to physician attitudes and knowledge concerning anticoagulation care. With regard to the delicate balance of benefits versus risks in oral anticoagulant therapy, some physicians tend to undertreat patients because they fear a bleeding complication, even at the expense of failing to prevent an ischemic stroke.[26,27] Also, lack of clear practice guidelines regarding optimal scheduling of INR tests may hinder delivery of optimal anticoagulation care by physicians, as described by Shalev et al.[28] In fact, significantly more patients in the poor-control group had an above-average number of INR determinations (43.5 % vs 25.9%, P = .001), which may indicate precariousness in anticoagulation care. This issue needs to be further explored, but it may relate to lack of adequate training in anticoagulation care among non–board-certified physicians.

Unfortunately, in our study, patients on warfarin therapy were within the recommended therapeutic range less than half the time. A number of studies both in the United States and in Europe evaluated the economic benefit associated with optimization of anticoagulation control among patients with AF.[8,29] Substantial cost savings stemmed mainly from stroke prevention but also from reduced hospitalization rates and emergency department visits.[30]

Table 3. Descriptive Statistics for Patients With Poor Anticoagulation Control, Good Anticoagulation Control, and Excellent Anticoagulation Control[a]

Characteristic	Anticoagulation Control[b]		
	Poor (n = 611, 67.4%)	Good (n = 187, 20.6%)	Excellent (n = 108, 11.9%)
Mean (SD) age, y	71.8 (9.3)[c]	72.4 (8.1)	69.7 (8.3)
Female	54.8[c]	47.6	42.6
More than 16 INR determinations	43.5[c]	45.5[c]	25.9
Stroke risk factor			
Age ≥75 y	46.8[c]	46.0[c]	31.5
Diabetes mellitus	30.6[c]	29.4[c]	16.7
Hypertension	82.2	79.7	76.9
Heart failure	45.3[d]	36.4	25.0
Prior stroke	20.3[c]	18.3[c]	7.4
Physician certification			
Not board certified	53.2[c]	47.0	40.2
Family medicine	36.1	42.5	45.1
Internal medicine	7.1	6.1	5.9
Geriatrics	3.4	4.4	7.8

INR indicates international normalized ratio; TTR, time within therapeutic range.
[a]Values are percentages within each group unless otherwise indicated.
[b]Poor anticoagulation control is indicated by TTR <60%; good anticoagulation control by TTR 60% to 75%; and excellent anticoagulation control by TTR >75%.
[c]P <.05 compared with the group with excellent anticoagulation control.
[d]P <.001 compared with the group with excellent anticoagulation control.

Table 4. Predictors of Poor Anticoagulation Control in a Multivariate Logistic Regression Analysis[a]

Patient Characteristic	Odds Ratio (95% CI)	*P*
Non–board-certified physician	1.41 (1.05-1.88)	.022
Heart failure	1.63 (1.20-2.22)	.002

CI indicates confidence interval.
[a]Variables included in the analysis were sex, age ≥75 years, diabetes, prior stroke, non–board-certified physician, and heart failure.

Since optimal anticoagulation control is desirable on both medical and economic grounds, ways to improve control should be sought. If good anticoagulation control cannot be achieved within the usual care setting, specialized anticoagulation clinics are a validated alternative option.[10] Moreover, innovative methods are being examined, some with promising results, such as handheld patient INR meters and computer-aided programs for warfarin maintenance.[31]

Despite the above-mentioned efforts, warfarin may not ultimately provide the optimal anticoagulation needed. Therefore, its substitution with newer oral anticoagulant drugs may eventually be inevitable. The direct thrombin inhibitor dabigatran, which abolishes the need for INR monitoring, has recently proved its efficacy and may be the anticipated substitute for warfarin.[32] As the newer anticoagulant drugs are associated with substantial expenditures, a careful cost–benefit analysis should be conducted to determine their feasibility.

Our study has several limitations. First, we were unable to acquire data concerning clinical outcomes such as stroke and bleeding event rates for our study population. For that reason, we elected to use anticoagulation control as a surrogate indicator for outcome, given the strong association between TTR levels and clinical outcomes.[6,7] Second, we could not assess scheduled interruptions of oral anticoagulants (ie, periprocedural, hospitalization), which may have resulted in underestimation of the TTR levels of the study group; however, a similar study estimated interruptions to cause a 5.6% decline in TTR levels, which does not alter the results considerably.[12] Finally, our population had a high burden of comorbidities, which may limit the study's generalizability to other settings, although anticoagulation control achieved in our study is similar to that found in a meta-analysis examining anticoagulation quality in patients with AF reported by Baker et al.[10]

CONCLUSIONS

This study provides important information about anticoagulation control of patients with AF who receive routine medical care within a large MCO. Overall, patients with AF had suboptimal control, with less than half the time spent within the therapeutic range, which placed them at heightened risk for medical complications, mainly stroke. Our results suggest that patient comorbidities and lack of physician board certification negatively affect anticoagulation control. Patients with AF who are treated in routine care could benefit from methods aimed at improving control; hence, further research is needed to assess cost-effectiveness of such methods.

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