Atrial Fibrillation: A Primary Care Cross-Sectional Study

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ABSTRACT: **Background:** Atrial fibrillation (AF) is the most common arrhythmia in adults and is associated with increased mortality and morbidity.

Objectives: To characterize patients diagnosed with AF in primary care clinics in southern Israel.

Methods: We conducted a cross-sectional study in 14 primary care clinics of the largest health insurance fund in Israel, reviewing the electronic medical records of adults aged ≥ 25 years diagnosed with AF. The prevalence, evaluation, antithrombotic treatment and treatments for rate control/rhythm control were analyzed.

Results: We retrieved the records of 995 patients with a diagnosis of AF; the prevalence of AF was 1.5% (2.5% aged ≥ 45 years). The patients' mean age was 73.5 ± 1.4 years and 55.3% were female. Vitamin K antagonist (VKA) was prescribed for 591 patients (59%), of whom 8.5% had no international normalized ratio follow-up tests for at least 3 months before our review. Among patients in the VKA treatment group the risk for thromboembolic events was considered to be high, moderate and low in 22% (n=131), 66% (n=391) and 12% (n=69), respectively. Patients with a low Congestive Hypertension Age Diabetes Stroke (CHADS2) score (odds ratio = 0.555, 95% confidence interval 0.357–0.862) and patients who did not receive VKA (OR = 0.601, 95% CI 0.459–0.787) received significantly less rate-control treatment. Of the patients with a low CHADS2 score (< 1) 52.7% received VKA treatment, and 39.4% with a high CHADS2 score (≥ 3) did not receive VKA. A positive correlation was found between anticoagulation and rate or rhythm control.

Conclusions: The prevalence and age distribution of AF in southern Israel are similar to findings in the western world. Many of the patients did not receive appropriate antithrombotic prophylaxis.

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KEY WORDS: atrial fibrillation, primary care, cross-sectional study, anticoagulation, rate control

Atrial fibrillation is the most common sustained arrhythmia in clinical practice. Its incidence increases with age, manifest as valvular heart disease (particularly mitral stenosis), ischemic heart disease, cardiomyopathy and hypertension [1-2].

The main complications of AF are heart failure exacerbation, cardiac ischemia, hypotension and thrombembolic events. In the Framingham study a significant increase in the incidence of stroke was noted among participants with AF [2]. Patients with valvular AF, especially rheumatic heart disease, had a 17-fold increase in the incidence of stroke, as compared to a fivefold and fourfold increase in patients with non-valvular and lone AF, respectively [3].

Several large studies and a meta-analysis provide a strong foundation supporting the use of anticoagulation therapy with the target international normalized ratio of 2–3 in patients with non-valvular AF who are at moderate to high risk for stroke and have a low risk of bleeding [4-6]. Two trials found that rate control and anticoagulation are at least as good as rhythm control, and medical treatment is the preferred option for most patients with AF [7].

Patients presenting with AF must be evaluated for their cardiac status, risk factors for AF complications and risk factors for bleeding, as well as monitoring of anticoagulation status and therapy. Numerous studies have evaluated the level of oral anticoagulation in patients with AF [4-16]. Most of these studies reported a high rate of under-treatment with oral anticoagulants in patients with AF, particularly in patients at high risk of stroke [8,10,11,14,15].

The aims of the present study were to identify patients in the community diagnosed with AF, and to assess the prevalence of AF diagnosis, the appropriateness of AF evaluation, the appropriateness and adequacy of the anticoagulation status therapy, and the use of rate and rhythm control.

PATIENTS AND METHODS

Clalit Health Services is the largest health fund in Israel, insuring 54% of the population. The study was performed during the years 2004–2006 in 14 Clalit primary care clinics with 99,925 listed patients; 66.6% were 25 years old or older.

OR = odds ratio
CI = confidence interval

AF = atrial fibrillation

All patients ≥ 25 years diagnosed with AF and listed in the study clinics were included. No validation of the AF diagnosis was performed. A diagnosis of AF in the patients' electronic medical record was accepted as AF. There was no differentiation in the EMR of the type of AF: paroxysmal, persistent, or permanent.

The information was extracted from the patients' EMR and included demography, comorbidities, medications, laboratory and diagnostic tests (thyroid-stimulating hormone, Holter, stress test, and echocardiogram). The anticoagulation data included the prescribed vitamin K antagonist, the frequency of follow-up tests, and INR levels during the previous 3 months.

Well-controlled INR was defined as INR within the target levels of 2–3 for at least 50% of the time. The thromboembolic risk was analyzed by using the CHADS2 score (congestive heart failure = 1, hypertension = 1, age > 75 = 1, diabetes = 1 and stroke = 2). The CHADS2 risk index [17] was calculated for each AF patient: two points were given for a history of stroke or transient ischemic attack, and one point for each of the following: age 75 years, and a history of hypertension, diabetes, or recent congestive heart failure. Each patient was categorized into one of three groups: low risk group with a CHADS2 score of 0 points, moderate risk group with a CHADS2 score of 1–2 points, or high risk group with a CHADS2 score of ≥ 3 points. Rate and rhythm control were assessed according to the pharmacy's purchasing database documentation. Patients treated with any anti-arrhythmic medication – propafenone, fecainide, sotalol or amiodarone – were categorized as following a regimen of rhythm control, all others as following a regimen of rate control.

STATISTICAL ANALYSIS

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software, version 15 (SPSS, Chicago, IL, USA). Chi-square tests were used to analyze statistically significant differences of categorical variables. Logistic regression models were used for multivariate analyses. Two-tailed *P* values < 0.05 were considered statistically significant, with power of 0.8.

RESULTS

Of the 99,925 patients listed in the 14 Clalit primary care clinics included in the study, 66,550 were over 25 years old. We found 995 records of patients with a diagnosis of AF (1.5%). AF characterization (paroxysmal, persistent, or permanent) was lacking; 59.4% (n=591) regularly received VKA therapy. The mean age was 73.5 ± 1.4 (range 28–101 years) and 55.3% were female. The observed comorbidity was hypertension in 70.3%, ischemic heart disease in 19.7%, congestive heart failure in 10.3%, and stroke in 9.7%.

VKA THERAPY

In our study group we found that the prevalence of AF increased with age: 0.03% were 25–44 years old, 0.7% were aged 45–64, 3.1% were 65–74, 6.5% were 75–85, reaching 9.3% of patients aged 85 and above. More patients receiving VKA treatment suffered from hypertension (62.5%), diabetes (66.5%) and rheumatic heart disease (80.6%) ($P < 0.01$). No gender differences were found in the VKA prescription rate (59.8% vs. 59.1%), although patients receiving VKA were younger (73.15 ± 9.74 vs. 74.13 ± 13.48, $P < 0.001$).

No significant differences in CHADS2 scores were found between the patients who received VKA and patients who did not. More patients who were not prescribed VKA suffered from anemia (58.1% vs. 41.9%, $P < 0.01$). No statistically significant differences were found between the prescribed/not prescribed VKA groups in the prevalence of duodenal ulcer and history of a bleeding disorder [Table 1].

Patients prescribed VKA treatment underwent a more extensive workup: thyroid-stimulating hormone (60.7% vs. 39.3%, $P < 0.01$), chest X-ray (66.0% vs. 34.0%, $P < 0.001$) and echocardiography (67.4% vs. 32.6%, $P < 0.001$). More patients underwent a pacemaker implantation (80.0% vs. 20.0%, $P < 0.001$). Aspirin was a concomitant treatment in 385 patients (38.7%).

VKA FOLLOW-UP

The number of INR test results and level of control in patients receiving VKA treatment is shown in Table 2. The average number of INR tests performed in patients taking VKA in the previous 3 months was 3.9 per patient. However, in 8.5% of the

Table 1. VKA treatment and risk scores

	VKA treatment					
	Yes (N=591)		No (N=404)			
	N	%	N	%	Total	*P* value
Comorbidity						
Hypertension	437	62.5%	262	37.5%	699	< 0.01
Diabetes	157	66.5%	79	33.5%	236	< 0.01
Rheumatic heart disease	29	80.6%	7	19.4%	36	< 0.01
Thyroid	109	66.1%	56	33.9%	165	0.056
Cancer	8	44.4%	10	55.6%	18	NS
Ischemic heart disease	125	63.8%	71	36.2%	196	NS
Cardiomyopathy	6	85.7%	1	14.3%	7	NS
Dyslipidemia	189	63.4%	109	36.6%	298	NS
	591		**404**		**995**	
CHADS2 risk group						
Low	69	52.7%	62	47.3%	131	NS
Moderate	391	60.3%	257	39.7%	648	
High	131	60.6%	85	39.4%	216	
	591		**404**		**995**	

EMR = electronic medical record
INR = international normalized ratio
CHADS = Congestive Hypertension Age Diabetes Stroke
VKA = vitamin K antagonist

Table 2. Anticoagulation follow-up in patients receiving VKA in the last 3 months

	N	%
Number of INR tests		
0	50	8.5
1–2	138	23.4
3–6	298	50.4
7–10	104	17.6
11+	1	0.2
Total	**591**	
Mean ± SD	3.9 ± 2.60	
Range	0–11	
INR tests results		
‹ 2	663	28.8
2.01–3	1127	49.0
≥ 3	510	22.2
Total	**2300**	
Time within target range (2<INR<3)		
50% of INR tests	325	55.0
66% of INR tests	189	32.0

VKA-treated patients no INR tests were performed during the whole study period. In 23.4% of the treated patients the number of INR tests performed in the previous 3 months was 1–2 per patient. Forty-nine percent of all INR tests were within the therapeutic range (2<INR<3). There were 325 patients (55%) within the therapeutic range 50% of the time, and only 189 patients (32%) were within the therapeutic range 66% of the time.

Patient refusal was the main reason (20.7%) for not receiving VKA. Other causes noted were dementia (13.5%), previous gastrointestinal bleeding (11.7%) and stroke (7.8%).

Table 3. Rate-control treatment and VKA rate and risk scores

	Rate control					
	Yes (n=660)		No (n=335)			
	N	%	N	%	Total	*P* value
Comorbidity						
Hypertension	484	69.2%	215	30.8%	699	0.003
Diabetes	167	70.2%	71	29.8%	238	0.158
Rheumatic heart disease	27	75.0%	9	25.0%	36	0.287
Thyroid	105	63.6%	60	36.4%	165	0.419
Cancer	9	50.0%	9	50.0%	18	0.206
Ischemic heart disease	129	65.8%	67	34.2%	196	0.866
Cardiomyopathy	7	100.0%	0	0.0%	7	0.103
Dyslipidemia	167	70.2%	71	29.8%	238	0.158
	660		**335**		**995**	
CHADS2 risk group						
Low	73	55.7%	58	44.3%	131	0.017
Moderate	436	67.3%	212	32.7%	648	
High	151	69.9%	65	30.1%	216	
	660		**335**		**995**	
VKA						
Received	421	71.2%	170	28.8%	591	0.001
Did not receive	239	59.2%	165	40.8%	404	
	660		**335**		**995**	

RATE-CONTROL TREATMENT

A total of 660 patients (66.3%) received rate-control treatment without anti-arrhythmic medications. This treatment included beta blockers (N=467, 47%), digoxin (N=129, 13%) and non-dihydroperidine calcium channel blockers (N=158, 15.9%). More patients ($P = 0.03$) receiving rate-control treatment suffered from hypertension (69.2%). No statistically significant differences were found in other comorbidities. More patients receiving rate-control treatment had higher CHADS2 scores than patients who did not receive the treatment (69.9% vs. 30.1%, $P = 0.02$). Almost 71% of the patients who received anticoagulation therapy also received rate-control treatment, compared with 59.2% of the patients who did not receive VKA therapy ($P < 0.001$) [Table 3]. Unfortunately, we do not know how many had paroxysmal, persistent or permanent AF.

Table 4 shows the results of two logistic regression models. The first model predicts AF patients who will receive rate-control treatment. Patients with low CHADS2 score (OR 0.555, 95% CI 0.357–0.862) and patients who do not receive VKA (OR 0.601, 95% CI 0.459–0.787) will significantly receive less rate-control treatment. To reflect age and gender adjustment, these variables remained in the model despite being not statistically significant. Contraindications and comorbidity variables were not statistically significant

Table 4. Logistic regression models

Variable	Odds ratio	95% confidence interval	*P* value
AF patients who will receive rate control			
Gender			
Male	1		
Female	0.773	0.588–1.016	0.065
Age (per year*)	0.992	0.978–1.005	0.992
Receives VKA			
Yes	1		
No	0.601	0.459–0.787	0.001
CHADS2 risk group			
Low	0.555	0.357–0.862	0.009
Moderate	1		
High	1.131	0.804–1.590	0.479
AF patients who will not receive VKA			
Gender			
Male	1.003	0.793–1.345	0.811
Female	1		
Age (per year*)	0.989	0.978–1.001	0.074
Comorbidity			
Yes	1.812	1.247–2.632	0.002
No	1		
Rate control			
Receive	1.660	1.268–2.175	0.001
Do not receive	1		

*Being older by one year lowers the chance of receiving/not receiving the treatment

and were excluded from the model. The second model predicts AF patients who will not receive VKA. Patients suffering from comorbidities (OR 1.812, 95% CI 1.247–2.632) and patients who were receiving rate-control treatment (OR 1.660, 95% CI 1.268–2.175) will receive significantly fewer VKA. Again, to reflect age and gender adjustment, these variables remained in the model despite being not statistically significant. Contraindications and CHADS2 risk score variables were not statistically significant and were excluded from the model.

DISCUSSION

Atrial fibrillation can significantly increase morbidity and mortality, with stroke being the most serious complication. Vitamin K antagonists are the mainstay of current practice for AF patients at moderate to high risk of stroke.

The just over 1.5% prevalence of AF is consistent with that found by other researchers [2]. An Italian study of patients with AF reported that 35% (n=75) of the patients in the high risk category were either not taking antithrombotic prophylaxis or were being treated with aspirin only [19].

Comparison with previous studies evaluating prescriptions and monitoring of anticoagulation in patients with AF show that our findings are very similar, suggesting that management of anticoagulation in AF patients is problematic worldwide. A review of more than 20 studies of patients with AF showed that only 15–44% of eligible patients were actually prescribed anticoagulation [18,20]. In our study, anticoagulation was prescribed to 59% of the AF patients. We also found that 8.9% of the AF patients who received VKA and 14.6% of the AF patients who did not had contraindications (anemia, duodenal ulcer, history of bleeding).

Our findings showed that 325 patients taking VKA (55%) were within their INR target range 50% of the time, 216 (36.5%) were not, and 50 patients (8.5%) did not have any follow-up test although they regularly received VKA therapy. In a review of 660 patients managed by general internists and family practitioners [7], the INR was within the target range in only 44% of the patients and below the target range in 38%.

In our study we found that the prevalence of AF increases with age, reaching 9.3% of the patients aged 85 and above. A study examining a general practice database in Britain found that the incidence of AF increased by age and was higher in men compared to women. Approximately 8% of the patients aged ≥ 85 years had AF [21]. A cross-sectional primary care study in Scotland observed that women and older individuals were less likely to be prescribed warfarin and more likely to be prescribed dogoxin than beta blockers or rate-limiting calcium channel blocker for rate control [22].

We also found that patients who did not receive VKA treatment were statistically significantly older (59.2% aged ≥ 75). However, no gender differences were found in the VKA prescription rate.

In our study no significant differences in CHADS2 scores were found between patients who received anticoagulants and patients who did not. A large study analyzing a computerized database of general practitioners in Britain (41,910 AF patients) found that when adjusting for age and gender there was no association between higher risk for stroke (CHADS2 score) and initiation of warfarin or aspirin, contrary to current guideline recommendations [23].

In our study 660 patients (66.3%) received rate-control treatment. This treatment consisted of beta blockers (47%), digoxin (13%) and non-dihydroperidine calcium channel blockers (15.9%). In a cross-sectional study of primary care practices participating in the Scottish Continuous Morbidity Recording Scheme between April 2001 and March 2002 [24], 71% of patients with AF received rate-controlling medication: beta blocker 28%, rate-limiting calcium channel blocker 42%, and digoxin 43%. We also found that patients with low CHAD2 score (OR 0.555, 95% CI 0.357–0.862) and patients who were not on VKA treatment (OR 0.601, 95% CI 0.459–0.787) receive significantly less rate-control treatment. We are aware that in some cases amiodarone can be used as a rate-control agent, and in others, rate-slowing drugs should be used as adjuvant in a rhythm-control regimen with type Ia and Ic anti-arrhythmic drugs. However, we believe this is a close estimation. We did not evaluate rhythm control achieved by electric cardioversion and rate-slowing drugs rather than chronic use of anti-arrhythmic drugs. In our study, of the 404 patients who did not receive VKA therapy, 69 (20.7%) refused to receive treatment, in 48 (14.4%) treatment was stopped following a cardiologist's recommendation, 45 (13.5%) suffered from dementia, and 39 (11.7%) had previous bleeding.

More patients ($P < 0.01$) receiving rate-control treatment suffered from hypertension (69.2%). No statistically significant differences were found in other comorbidities. More patients receiving rate-control treatment had higher CHADS2 scores than patients who did not receive the treatment (69.9% vs. 30.1%, $P = 0.02$).

Although many clinical trials showed that anticoagulation reduces the risk of ischemic stroke in patients with AF, even when anticoagulation is prescribed, maintaining the goal INR is often not achieved. Possible explanations for this underuse may be doubts about the effectiveness of anticoagulation, the fear of hemorrhagic complications such as intracerebral bleeding, and the limitations of its use – such as frequent coagulation monitoring and interactions with food, alcohol and other drugs. Patient self-testing and self-management has been shown to improve the accuracy and quality of oral anticoagulation [10] and may improve quality of life. This study found that about 50% of AF patients at high risk for

stroke either did not receive anticoagulation therapy or were receiving insufficient anticoagulation.

Support and training for the complex task of anticoagulation management, as well as improved communication between all those involved – namely patients, physicians and anticoagulation therapy centers – may offer AF patients better protection from cerebrovascular accidents through appropriate prophylactic anticoagulation therapy.

With regard to the strengths and limitations of the study: This was a large retrospective study that evaluated the electronic records of patients with AF. Yet the type of AF (paroxysmal, persistent, or permanent) could not be defined. The study's objective was to evaluate the prevalence of AF diagnosis and its treatments, although the diagnosis itself was not validated. We used the recent anticoagulation criteria to evaluate the appropriateness of the treatment; however, we did not always have the data on the duration of the anticoagulation treatment.

The evaluation and use of antithrombotic prophylaxis are less than optimal. Numerous methods have been reported to be useful in the American and European health care setting to improve control. These include the establishment of specialized anticoagulation clinics, point-of-care patient self-testing, and computerized algorithms for anticoagulation dose adjustment [25].

As our population ages, combined with the increase in frequency of AF with age, the burden of AF is likely to increase in the future. Clearly, better data definitions and enhanced provider education are necessary to improve adherence. Other obstacles to enhanced adherence to anticoagulation guidelines in AF patients include the difficulty administering and monitoring anticoagulation and the lack of structured programs such as anticoagulation clinics. Patients should be thoroughly educated about the rationale for anticoagulation before starting this treatment. Thus, ongoing encouragement of the medical community to intensify anticoagulation treatment in patients with atrial fibrillation is required.

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