Background: Information on the prevalence and real-life management of atrial fibrillation (AF) in a general practice setting is sparse.

Objectives: To investigate the prevalence, clinical features and real-life management of AF in ambulatory consultant cardiology clinics.

Methods: We studied consecutive new patients with a diagnosis of AF. Recorded data included demographics, comorbidities and prescribed drugs. Antithrombotic therapy was chosen according to CHADS2 score in non-rheumatic valve AF patients; for AF patients with rheumatic valve disease warfarin treatment was prescribed. The data were compared with data of patients without AF admitted to the ambulatory cardiology clinics during the same period.

Results: The study included 865 patients whose mean age was 64.9 ± 7.1 years. AF was reported in 137 patients (15.8%); 81 were women (59%) and the mean age was 74.4 ± 7.5 years. Heart rate rhythm-control strategy was applied in 41 patients (45%) and rate control in 50 patients (55%) with paroxysmal or persistent AF. Rate-control strategy was used in all patients with permanent AF. In most patients AF was associated with one or more concomitant comorbidities, most frequently hypertension. Warfarin was prescribed in 98 patients with AF (71.5%), aspirin in 57 patients with AF (41.6%), and both drugs in 18 patients with AF. Amiodarone was used in 24 patients with AF (17.5%); beta blockers were used in 95 patients with AF (69.3%) and 377 patients without AF (51.8%).

Conclusions: We provide a snapshot of real-life contemporary daily clinical practice and evaluate AF burden and therapy. Most patients were found to have AF associated with one or more concomitant comorbidity.

KEY WORDS: atrial fibrillation (AF), ambulatory cardiac clinic, stroke risk factor, rate-control strategy, rhythm-control strategy

For Editorial see page 313

Atrial fibrillation is the most common arrhythmia in clinical practice and is an extremely costly public health problem [1]. In contrast to the considerable interest in AF in population-based and hospital studies [2-10], information on the prevalence and real management of AF in a general practice setting is limited. Moreover, most of the studies that do exist [11-13] were performed before publication of American College of Cardiology/American Heart Association/European Society of Cardiology guidelines [14]. We therefore investigated the prevalence, clinical features and real-life management of AF in ambulatory consultant cardiology clinics.

PATIENTS AND METHODS

We studied consecutive new patients with a diagnosis of AF sent to our ambulatory cardiology clinics over a 3 month period. To be included in the study, patients had to be in AF and/or have a history of AF with AF episodes documented by electrocardiogram, treated or untreated. The AF was classified according to the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with AF [14].

The recorded information included demography, comorbidities and prescribed drugs. Antithrombotic therapy was chosen according to CHADS2 score [14] to prevent stroke in AF patients with non-rheumatic valve. Warfarin was initiated in patients with CHADS2 score ≥ 2, and a target international normalized ratio of 2–3. Aspirin at a dose of 100 mg/day or warfarin as prescribed by the physician were administered in patients with CHADS2 score < 2. In all AF patients with rheumatic valve disease, warfarin treatment was prescribed with a recommended INR of 2.5–3. Warfarin treatment was supported by an anticoagulation clinic to monitor the INR. The comparison group comprised patients without AF admitted to the ambulatory cardiology clinics during the same period.

STATISTICAL ANALYSIS

Categorical variables were compared by chi-square test or Fisher’s exact test, as appropriate. Continuous variables, reported as mean ± SD, were compared by Student’s t-test. A P value < 0.05 was considered statistically significant.
The study included 865 patients: 400 women (46.2%) and 465 men (53.8%); their mean age was 64.9 ± 7.1 years. The clinical characteristics of the patients are reported in Table 1. AF was reported in 137 patients (15.8%); paroxysmal AF was diagnosed in 56 patients (40.8%), persistent AF in 35 patients (25.6%) and permanent AF in 46 patients (33.6%). Lone AF was reported in 9 patients (6.6%). AF was reported in 81 women (59%) and 56 men (41%). The mean age of the patients with AF was 74.1 ± 7.5 years; their age distribution is summarized in Figure 1. One hundred patients with AF (71.5%) and target INR was reached in 76 patients (77.5%). Aspirin was given to 57 patients with AF (41.6%); 18 patients received warfarin and aspirin. Antithrombotic treatment in patients with AF according to CHADS2 score is summarized in Figure 2. CHADS2 score ≥ 2 was found in 105 patients (76.6%): 86 of them (81.9%) received warfarin; 19 (18.1%) were not treated with warfarin for the following reasons: poor compliance in 3 patients, 3 patients had previous gastrointestinal bleeding, 2 patients had malignant neoplasm, 3 patients had recurrent falls, and 8 patients refused warfarin treatment. CHADS2 score < 2 was found in 22 patients (16.1%): 13 patients (59.1%) received aspirin and 9 patients (40.9%) warfarin. AF with concomitant significant valve disease was present in 23 patients (16.8%); 10 patients had rheumatic valve disease (8 patients post-mitral and/or aortic valve replacement and 2 patients with moderate mitral stenosis).

**RESULTS**

Of the 17 patients with AF and thyroid disease, 6 patients (35.3%) had amiodarone-induced hypothyroidism. Arrhythmias other than AF were diagnosed in 43 patients (5%). Details of the drug therapies at the clinic visit are provided in Table 2.

Rhythm control was applied in 41 patients (45%) and rate control in 50 patients (55%) with paroxysmal or persistent AF. In all 46 patients with permanent AF the rate-control strategy was used. Warfarin was prescribed in 98 patients with AF (71.5%) and target INR was reached in 76 patients (77.5%). Aspirin was given to 57 patients with AF (41.6%); 18 patients received warfarin and aspirin. Antithrombotic treatment in patients with AF according to CHADS2 score is summarized in Figure 2. CHADS2 score ≥ 2 was found in 105 patients (76.6%): 86 of them (81.9%) received warfarin; 19 (18.1%) were not treated with warfarin for the following reasons: poor compliance in 3 patients, 3 patients had previous gastrointestinal bleeding, 2 patients had malignant neoplasm, 3 patients had recurrent falls, and 8 patients refused warfarin treatment. CHADS2 score < 2 was found in 22 patients (16.1%): 13 patients (59.1%) received aspirin and 9 patients (40.9%) warfarin. AF with concomitant significant valve disease was present in 23 patients (16.8%); 10 patients had rheumatic valve disease (8 patients post-mitral and/or aortic valve replacement and 2 patients with moderate mitral stenosis).

**DISCUSSION**

In the present study the prevalence of AF (16.1%) was higher than previously reported among emergency admissions in
a general district hospital (6.2%) [2], in an acute general medical unit (10.4%) [3], among admissions in a cardiology department (9.8%) [10], and in general practice (2.4%) [11]. These differences, however, may depend on selection bias when recruiting the patients.

AF was the most frequent arrhythmia encountered in our ambulatory cardiology clinics, being present three times more frequently than all other arrhythmias combined. Patients with AF were older than those without AF; AF prevalence increased sharply from age 70, in accordance with other reports [5,13]. In the literature, the prevalence of AF is reported to be higher in men than in women [6,9]. In our study, this was only true in men younger than 70 years. The prevalence of AF in women over 70 was higher than that in men over 70, in agreement with other reports [15,16].

Patients with AF were associated with a variety of comorbidities, similar to patients without AF. In accordance with other studies, hypertension was confirmed as the most frequently associated comorbidity in AF patients [4,8,16,17]. Congestive heart failure, significant valve disease, and thyroid disease were more predominant in patients with AF than in those without, as reported by others [17]. In about one-third of patients with AF, thyroid disease was induced by iatrogenic amiodarone.

Four types of AF have been suggested [14]: a) first detected episode, b) paroxysmal, c) persistent, and d) permanent. The European Society of Cardiology new guidelines for the management of AF [18] introduced a fifth type: long-standing persistent AF, when AF lasts for 1 year or more. Patients in this category are considered candidates for ablation therapy [16]. The types of AF are not mutually exclusive and, retrospectively, doubts are likely to arise in the attribution to the different AF patterns because current treatments may change the natural course of AF. However, to date, misclassifications have been infrequent [4]. There were no patients with a first detected episode in our study population, most probably because of the type of patients referred to ambulatory cardiology clinics. Paroxysmal AF was the most frequent pattern, while persistent AF was the least frequent. Other authors [4,8,16] have reported permanent AF to be the most frequent type and persistent AF to be the least frequent, as in our series. Lone AF was seen in a small percentage of our patients, lower than the percentages reported by others [4,8,16,17].

According to ACC/AHA/ECS guidelines [14], rate control is a reasonable strategy in elderly patients with minimal symptoms related to AF. Elderly patients represented about three-quarters of our study population and rate-control strategy was used with 70% of them. Other studies refer to a lower percentage of use of rate-control strategy [4,7,17]. However, in the last 10 years, there has been a continual rise in the use of rate-controlling medications [18], most probably because the available rhythm-control strategies are inadequate. We are currently in need of safer and more efficacious anti-arrhythmia drugs for the control of AF [4].

Beta blockers, angiotensin-converting enzyme inhibitors and statins were the most frequently used drugs. Beta blockers were used by nearly all patients assigned to the rate-control strategy, in agreement with others [19,20]. Digitalis was prescribed more frequently in patients with AF than in patients without AF, but less than in Europe [4]. Anti-arrhythmic agents were used in less than one-third of the patients with AF, with amiodarone being the most frequently used drug; similar results were reported recently [17].

Risk of stroke was estimated based on CHADS2 score, because this scoring system is simple, easy and efficient. It has been reported that anticoagulation remains significantly underused in the real-world clinical setting for hospitalized patients with AF [21-23]. However, it has been verified that studies utilizing administrative databases and ICD-9 CM coding might be overestimating the underutilization of warfarin [24]. In this study, 81.9% of the patients with CHADS2 score ≥ 2 received warfarin, i.e., less than 88% of the patients reported by Meiltz et al. [8] but more than 71.4% and 67% of the patients reported by Nabauer et al. [16] and in the Euro Heart Survey [4], respectively. Conversely, anticoagulant treatment was prescribed in 40.9% of the patients with CHADS2 score < 2; similar overtreatment for stroke in low risk patients has been reported by others [4,8,16]. These data represent an over-interpretation of the current guidelines in low risk patients. In patients with CHADS2 score of 0–1, the new ESC guidelines [18] recommend using the CHA2DS2-VASC score, which is a more comprehensive estimator of risk factor for the thromboembolism-based approach than that evaluated by the CHADS2 score. New anticoagulant drugs for stroke prevention in AF have been developed and are under investigation; the efficacy of dabigatran has already been confirmed in the RE-LY study [24]. We believe that these drugs will ease the management of AF patients for the prevention of strokes compared to warfarin.

LIMITATIONS

Our study was confined to only a few ambulatory clinics, and practices may vary at other ambulatory centers. A follow-up was not performed, and since AF is a progressive disease [25] and its treatment varies in daily cardiology practice, changes in AF type, therapy and prognosis could not be determined. We could not collect data to verify the effects of oral anticoagulant therapy in preventing strokes or causing major bleeding.

CONCLUSIONS

This study presents a snapshot of real-life contemporary clinical practice and evaluates AF burden and therapy in daily clinical practice. Most patients were found to have AF associated with one or more concomitant comorbidity, most
frequently hypertension. The collected data represent a tool for surveying and helping to improve routine clinical care.

Corresponding author:
Dr. D. Antonelli
Dept. of Cardiology, HaEmek Medical Center, Afula 18101, Israel
Phone: (972-7) 649-4246
Fax: (972-3) 659-1444
email: antonelli_dante@hotmail.com

References

Capsule

Tissue factor and PAR1 promote microbiota-induced intestinal vascular remodelling

The gut microbiota is a complex ecosystem that has co-evolved with host physiology. Colonization of germ-free (GF) mice with a microbiota promotes increased vessel density in the small intestine, but little is known about the mechanisms involved. Tissue factor (TF) is the membrane receptor that initiates the extrinsic coagulation pathway, and it promotes developmental and tumor angiogenesis. Reinhardt et al. show that the gut microbiota promotes TF glycosylation associated with localization of TF on the cell surface, the activation of coagulation proteases, and phosphorylation of the TF cytoplasmic domain in the small intestine. Anti-TF treatment of colonized GF mice decreased microbiota-induced vascular remodelling and expression of the proangiogenic factor angiopoietin-1 (Ang-1) in the small intestine. Mice with a genetic deletion of the TF cytoplasmic domain or with hypomorphic TF (F[-/]) alleles had a decreased intestinal vessel density. Coagulation proteases downstream of TF activate protease-activated receptor (PAR) signalling implicated in angiogenesis. Vessel density and phosphorylation of the cytoplasmic domain of TF were decreased in small intestine from PAR1-deficient (F2r/-) but not PAR2-deficient (F2r/−) mice, and inhibition of thrombin showed that thrombin–PAR1 signalling was upstream of TF phosphorylation. Thus, the microbiota-induced extracellular TF–PAR1 signaling loop is a novel pathway that may be modulated to influence vascular remodelling in the small intestine.

Nature 2012; 483: 627
Eitan Israeli