Original Research

Management of Atrial Fibrillation in the Greek Healthcare Setting

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Introduction: Atrial fibrillation (AF) is the most frequent cardiac arrhythmia in the general population. AF management patterns have important implications for both the patient's quality of life and the utilisation of healthcare resources. This study aimed to investigate the management pattern of AF among cardiologists in the Greek healthcare setting.

Methods: In order to construct the outpatient management model, the patient record data of 149 geographically distributed physicians were used. Data on inpatient resource utilisation were obtained from a consensus panel of AF experts.

Results: 89.6% of AF patients were treated with pharmacological agents, whereas 5.2% of patients were treated with invasive methods and 5.2% received no treatment. In 59.5% of patients under pharmacological therapy, a rhythm-control strategy was implemented, whereas for the remaining 40.5% of patients a rate-control strategy was selected. Class Ic and III antiarrhythmic agents constituted the main therapeutic choices in the rhythm-control strategy, whereas β-blockers and digoxin were the most frequently prescribed agents in the rate-control strategy. 89.0% of the patients on pharmacological rhythm control, 91.3% of those on pharmacological rate control, and 100.0% of patients undergoing invasive treatment received antithrombotic medication.

Conclusions: Elimination of the rhythm disturbance and rhythm management are the dominant choices in AF management made by cardiologists in Greece. AF management requires close patient monitoring, as is reflected in the frequency of follow-up visits and laboratory tests performed, irrespective of treatment approach. Hospitalisations due to AF or related comorbidities are also common.

Atrial fibrillation (AF) is the most frequent form of cardiac arrhythmia in the general population and is associated with increased morbidity and mortality.[1] AF patients present a higher risk of acute myocardial infarction and congestive heart failure, whereas in highly symptomatic patients AF adversely affects their quality of life.[2-5]

Cardiovascular disease, hyperthyroidism, diabetes mellitus and high alcohol consumption are primary risk factors for AF. Recent studies have revealed additional risk factors, such as obesity, metabolic syndrome, diastolic dysfunction, sleep apnoea, stress, and genetic disposition.[4-8] The prevalence of AF is estimated to be 1% in the general population; however, there is a steep increase in AF prevalence in older age groups, reaching 10% in the population over 80 years old.[9-11] In the future, the number of patients with this arrhythmia is expected to rise significantly. Hypothesising a stable AF incidence rate, it has been estimated that the disease prevalence in the US will have tripled by 2050.[10,12] Data regarding the epidemiology of AF in Greece and the characteristics of the patients are limited.[13] Goudevenos et al,[14] in their study of paroxysmal AF in

north-western Greece, reported a mean annual incidence of paroxysmal AF of 6.2/10,000/year. AF occurrence was found to be higher for men (7.2/10,000/year) than for women (5.3/10,000/year). A study of the prevalence of permanent AF in subjects older than 65 years residing in a rural area[15] found a prevalence of 5% in that population. More recent publications[13] estimate the overall AF prevalence to be 3.9% in the general population.

The long-term management of AF includes the following therapeutic goals: control of the ventricular rate, correction of the rhythm disturbance and prevention of thromboembolism. Symptom relief and the management of concomitant cardiovascular disease should also be included in the therapeutic management goals.[16] We can differentiate between the pharmacological and non-pharmacological treatment of AF. Pharmacological treatment includes administering heart-rate controlling agents and/or antiarrhythmic agents. A combination of both is also very common, as many pharmaceuticals have both rate-controlling and antiarrhythmic properties. According to the clinical guidelines,[16] anticoagulation is necessary in either approach.

A better understanding of the mechanisms causing AF and the concurrent search for alternative treatments to pharmaceuticals have led to the introduction in clinical practice of various techniques, such as catheter ablation, ablation of the pulmonary node, pulmonary vein isolation, cardiac pacing, and surgery. These techniques are most commonly applied in cases when management of AF with pharmaceuticals does not achieve the therapeutic targets.[17]

Recently, a number of studies have been published with the purpose of depicting the everyday management of AF and, in some cases, comparing the cost and health outcomes of the rate- and rhythm-control strategies.[18-23] To our knowledge, the only data available regarding the management and cost of AF in Greece are the Euroheart Survey data.[20,24] The Euroheart Survey collected data from a sample of hospital outpatient and inpatient clinics. The present study aims to complement the previous research, presenting the disease management model for AF among cardiologists in both the inpatient and the outpatient setting in Greece.

Methods

Since centralised patient record databases are not available in the Greek National Health System,[25] our analysis of the management of AF patients in the out-

patient setting was based on a retrospective review of the patient records of 149 cardiologists. The sample was stratified according to geographical region and employment setting (cardiologists employed in public hospitals, social insurance funds and private practitioners). The required sample size was defined based on the methodology of estimating sample sizes for small populations,[26] i.e. using the normal approximation to the hypergeometric distribution, taking into account the total number of cardiologists in Greece (n=2820) and following the most conservative approach (largest sample) for an acceptable margin of error.

Participants were asked to review their patient records and complete a questionnaire regarding management and resource utilisation for the treatment of their AF patients. Patients were eligible for consideration in the study if they were ≥18 years old and diagnosed with AF for >1 year. The data concerned pharmaceuticals prescribed, average annual frequencies of consultations and laboratory/diagnostic tests performed, as well as the percentage of patients hospitalised for cardiovascular complications, AF, and adverse drug reactions.

In order to construct the patient management model, participants were requested to classify their patients according to basic treatment strategy, i.e. pharmacological treatment (rhythm control, rate control), and non-pharmacological treatment (catheter ablation, pacemaker implantation, surgical procedure). Discrete sets of answers were requested for all patient groups. The timeframe for the analysis was set to a one-year retrospective period, with 2010 as the baseline year. Data were analysed using SPSS v.17.0 and descriptive statistics are reported.

Parameters relating to hospital resource utilisation were approached using expert opinion in the form of a consensus panel.[27] The methodology was similar to the classical model of consensus procedures, as described by Allen et al.[28] The expert group consisted of 10 heads of cardiology clinics in the Greek National Health System (6 university and 4 general hospitals).

Results

The cardiologists designated 51.0% of their patients as having permanent AF, 30.0% were designated as having paroxysmal AF, and 19% as having persistent AF. The mean age was 53.2 ± 8.5 years, 59.9 ± 8.8 years, and 68.5 ± 7.6 years, for patients with paroxysmal, persistent and permanent AF, respectively.

Of the overall patient population, 89.6% were pre-

scribed pharmacological treatment as the initial choice. Of these, 59.6% were administered antiarrhythmic medication as part of a rhythm-control approach, while 40.5% were on medication with the primary purpose of controlling the ventricular rate; 5.2% of all patients were given non-pharmacological treatment using any of the available techniques (catheter ablation, pacemaker implantation, surgery), while 5.2% of all patients did not receive either treatment.

Pharmacological treatment

Class Ic or III antiarrhythmics were chosen for the majority of patients for whom control of the rhythm disturbance was the main treatment strategy, and were each administered to 28.9% of patients (Table 1). Class II antiarrhythmics were prescribed to 12.7% of patients, while 13.4% received a combination of antiarrhythmic agents. Oral anticoagulant therapy was prescribed in 89.0% of patients under pharmacological rhythm control. Regarding the antithrombotic agents prescribed, 73.1% of patients were prescribed coumarins, 21.9% antiplatelets, and 5.0% were prescribed both antithrombotic agents.

As is shown in Table 1, in 37.0% of patients under pharmacological rate control, β-blockers were the preferred agents. Digoxin was used in 24.4% of patients, while the percentage of patients receiving

a combination of rate-control pharmaceuticals was 21.6% — higher than the respective percentage in the rhythm-control group. The percentage of patients under pharmacological rate control who also received oral anticoagulation was 91.3%. Again, the majority (76.7%) of patients were treated with coumarins, 18.8% were treated with antiplatelet agents and 4.5% with both coumarins and antiplatelets.

In the patient group for whom a non-pharmacological approach was chosen (of whom almost 100% underwent catheter ablation), 89.0% were administered antiarrhythmic medication. The respective percentages are presented in Table 1.

The percentage of patients receiving prophylactic antithrombotic treatment in this patient group varied from 96.0% to 100.0% depending on the type of technique selected. Coumarins were the most commonly prescribed pharmaceuticals.

Follow up

As shown in Table 2, monitoring of the international normalised ratio (INR) was the most frequent laboratory test, irrespective of treatment strategy. The test was performed approximately monthly. INR measurements, together with electrocardiograms (performed about once every 3 months) and renal function tests (performed about once every 6 months)

Table 1. Pharmaceuticals prescribed for the treatment of AF, according to treatment strategy (n=149).

Pharmaceutical agents	% of patients (mean ± SD)
Pharmacological rhythm-control strategy:*	
Class Ia antiarrhythmics	5.5 ± 15.6
Class Ic antiarrhythmics	28.9 ± 25.5
Class II antiarrhythmics (except sotalol)	12.7 ± 14.9
Class III antiarrhythmics	28.9 ± 21.9
Class IV antiarrhythmics	3.3 ± 6.0
Digoxin	5.4 ± 11.9
Combinations	13.4 ± 21.7
Other	1.7 ± 8.4
Pharmacological rate-control strategy:	
Digoxin	24.4 ± 22.6
β-blockers	37.0 ± 23.7
Calcium channel blockers	14.7 ± 13.4
Combinations	21.6 ± 21.9
Other	2.6 ± 7.0
Antiarrhythmic agents prescribed in patients who underwent catheter ablation:	
Class Ic antiarrhythmics	20.0 ± 18.9
Class III antiarrhythmics	78.5 ± 52.2
Digoxin	1.5 ± 3.1

*Vaughan Williams classification of antiarrhythmic agents.

Table 2. Reported annual frequencies of consultations with a cardiologist and laboratory/diagnostic tests, in relation to treatment strategy.

	Pharmacological rhythm-control strategy (n=149)	Pharmacological rate-control strategy (n=149)	Non-pharmacological treatment (n=149)
Complete blood count	1.8 ± 0.76	1.9 ± 0.80	1.7 ± 0.93
Renal function tests*	1.9 ± 0.88	1.9 ± 0.86	1.7 ± 1.00
Thyroid function tests*	1.4 ± 0.63	1.4 ± 0.69	1.2 ± 0.78
Liver function tests	2.0 ± 1.53	2.0 ± 1.18	1.8 ± 1.55
INR monitoring*	10.0 ± 5.40	11.5 ± 5.99	8.3 ± 5.64
Electrocardiogram	4.2 ± 2.74	4.4 ± 2.96	4.0 ± 3.29
Holter monitoring	1.6 ± 1.27	1.4 ± 1.34	1.4 ± 1.01
Exercise stress testing	0.9 ± 0.55	0.8 ± 0.59	0.9 ± 0.60
Echocardiogram	1.4 ± 0.70	1.4 ± 0.71	1.3 ± 0.80
Pulmonary assessment*	0.9 ± 0.54	0.9 ± 0.60	0.8 ± 0.63
Consultations*	4.3 ± 3.49	4.0 ± 2.92	3.1 ± 2.85

*Statistically significant differences among groups at the 0.05 level. INR – international normalised ratio.

were the three most frequently performed tests. The average annual frequency of follow-up visits to the cardiologist was 4 for patients managed with a pharmacological treatment strategy and three for patients in a non-pharmacological treatment strategy.

Hospitalisation

As mentioned above, the study also examined the frequency of hospitalisations among AF patient groups. The percentages of patients hospitalised and the average numbers of admissions per year are presented in Table 3 according to treatment strategy and to the three selected reasons for admission: namely AF recurrence, AF-related cardiovascular complications, and drug adverse events.

Hospitalisations due to AF recurrence were more frequent in the pharmacological rhythm-control group and the group of patients treated with invasive techniques. Patients in these groups were admitted on average twice a year and four times a year, respectively. Hospitalisation due to AF-related cardiovascular complications was also less frequent in patients in the pharmacological rate-control strategy than in the other two patient groups. Finally, although the percentage of patients admitted to a hospital due to drug adverse events was relatively low, the mean number of admissions was high in all patient groups.

Discussion

The results of this study indicate that the principal treatment choice among Greek cardiologists for the management of AF patients is pharmacological treatment, mainly with the primary goal of correcting the rhythm disturbance (56.0% of patients under pharmacological treatment). Antiarrhythmic agents prescribed under this approach include Class Ic and Class III antiarrhythmics. Rate-control therapy was used in 40.5% of patients under pharmacological treatment, with β-blockers and digoxin being the treatments of choice. The percentage of patients receiving a combination of drugs was higher in this patient group than in the rhythm-control group.

AF management has also been described by national[29,30] as well as international surveys. Our findings are similar to those noted in the recently completed multi-centre observational RecordAF study.[23] In the RecordAF study, 55.0% of AF patients underwent rhythm control with the use of Class III antiarrhythmics and β-blockers, while in the rate-control strategy, patients were more frequently prescribed β-blockers and cardiac glycosides.

A direct comparison of our findings with those of previous studies[20,22] regarding physicians' choice between the rhythm- and rate-control strategies is challenging, because of differences in the definitions used. However, it is worthy of note that the percentage of patients undergoing invasive treatment noted in our study (5.5%) is similar to that reported for Greece in the Euroheart survey (5.9%).[24]

The percentage of patients receiving anticoagulation treatment exceeded 90.0% in all patient groups (pharmacological rhythm- and rate-control, non-pharmacological treatment). The corresponding percentage was 92% in Euroheart[31] (for all country set-

Table 3. Reported hospitalisation rate due to recurrence of atrial fibrillation (AF), AF-related cardiovascular disease complications, and drug adverse events per patient group.

Reason for hospitalisation	Pharmacological rhythm control		Pharmacological rate control		Non-pharmacological treatment	
	% of patients admitted	Average admissions/year	% of patients admitted	Average admissions/year	% of patients admitted	Average admissions/year
AF recurrence	20.0	2.0	6.0	1.4	18.8	4.0
AF-related cardiovascular complications	13.0	1.5	6.1	1.4	3.0	2.4
Drug adverse events	5.6	2.8	4.0	2.4	4.9	3.2

tings), 85.0% in the COCAF study[19] and 87.0% in the AFNET study.[22] Coumarins are the pharmaceutical agents of choice among Greek cardiologists. As expected, all patients who underwent invasive treatment were prescribed anticoagulants.

Another major finding in our study was that in the Greek healthcare setting, AF management involves frequent monitoring and performing of laboratory tests. The mean number of consultations (4 per year) was double the frequency reported for Greece in the Euroheart[24] survey (2 per year). This finding relates to the differences in the study samples. Whereas in Euroheart[24] participating centres were mainly specialised hospital clinics, the present study drew its sample from all types of healthcare providers. The observed differences may therefore imply a different management pattern between cardiologists practising in the hospital setting and cardiologists in primary health care.

Regarding admissions to a hospital due to AF related causes (AF recurrences, AF-related cardiovascular events, adverse drug reactions), our results indicate that the percentage and frequency of hospital admissions are higher in patients who are managed with a pharmacological rhythm-control strategy. A similar profile was also found in patients who were treated invasively. In the present study, almost all those patients underwent catheter ablation. Catheter ablation is the preferred option for young, highly symptomatic patients who are suffering mostly from paroxysmal rather than persistent AF.[17,32-33] However, the effectiveness of both currently available antiarrhythmic medications and ablation techniques in preventing AF recurrences has been found to be limited.[17,33] We can therefore conclude that the limitations of the aforementioned therapeutic options provide an explanation for the frequent admissions to hospitals due to AF recurrence in those groups of patients in our study.

This study was designed to provide information about the "real-life" management of AF. It should be noted that the data presented refer to the management of AF and do not include the management of comorbidities. In this context, data concerning pharmacotherapy, laboratory tests and consultations related to concomitant diseases are not included. Certain limitations apply to the study. Due to the lack of patient record data at a country-wide level a short-term retrospective analysis of patient records among a selective group of cardiologists was carried out. The method of choice in this case, i.e. the use of a multipoint data collection process, produced the highest possible validity of the outcomes, in the absence of other alternatives.

In conclusion, this study provides a unique snapshot of the actual clinical management and therapy of AF by cardiologists in all types of settings in the Greek healthcare system. Our results demonstrate that rhythm control for the long-term management of AF is the initial treatment choice of the majority of cardiologists in Greece. Regardless of treatment strategy, the percentage of patients receiving anticoagulation is considered satisfactory, compared to the results of similar studies in other country settings. Another important finding relates to the need for close monitoring of AF patients, which is reflected in the frequencies of annual consultations and laboratory tests requested.

Acknowledgements

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