A survey on the treatment of atrial fibrillation in South Africa

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Background. The burden of cardiovascular disease is expected to escalate in developing countries. However, studies and guidelines concerning atrial fibrillation (AF) are restricted to the developed world.
Objectives. To assess the treatment modalities of AF in South Africa.
Methods. A cross-sectional, observational, multicentre, national registry of the treatment of 302 patients with AF was conducted from February 2010 to March 2011. Specific drug use for rate or rhythm control, as well as drug use for stroke prevention, was surveyed. Events during the 12 months prior to the survey were also characterised, including non-drug treatments, resource utilisation and complications.
Results. The single most prevalent clinical characteristic was hypertension (65.9%). Rhythm control was being pursued in 109 patients (36.1%) with class Ic and class III antiarrhythmic agents, while rate control, mainly with beta-blockers, was pursued in the remainder of the patients. Concomitant use of other cardiovascular drugs was high, and 75.2% of patients were on warfarin for stroke prevention. There was a high burden of AF-related morbidity during the preceding year, with 32.5% reporting a history of heart failure, 8.3% a stroke and 5.3% a transient ischaemic attack. Therapeutic success, as defined by either the presence of sinus rhythm or rate-controlled AF, was achieved in 86.8% as judged clinically by the treating physician, but in only 70.2% according to the electrocardiogram criterion of heart rate ≤80 bpm.
Conclusion. There were no striking differences from previously reported registries worldwide. The lack of application of strict rate control criteria is highlighted.

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Atrial fibrillation (AF) is the most common cardiac arrhythmia, with a prevalence of 5 - 6% in the 65-year-old population, increasing up to 10% in the >80 years population.[1-4]

Despite the improvement in primary and secondary prevention of predisposing underlying cardiac conditions such as ischaemic heart disease and hypertension, the prevalence of AF continues to rise in developed countries due to ageing and increasing obesity of the population.[3,5,6] The treatment of AF is undergoing significant revision throughout the world and in a number of ways, especially with regard to stroke prevention, ablation for rhythm control, and novel antiarrhythmic drugs. This has triggered a number of guidelines[7,8] and guideline updates,[9,10] as well as a number of registries and surveys on AF and AF management in various parts of the world (e.g. Nieuwlaat *et al.*[11] and Camm *et al.*[12]). In South Africa (SA), the prevalence of AF in the urban black population has recently been documented to be 7% in a cardiovascular disease cohort (8% of heart failure patients, 4% of hypertensive patients, and 13% of valvular disease patients).[13] However, very little has been published on AF management outside the developed world. This prompted the Assessment of the Therapeutic Management of Patients with Atrial Fibrillation in South Africa (SAFIR-RSA). The principal objective of the study was to assess the baseline characteristics of patients with AF and the treatment modalities utilised, particularly the use of rate and rhythm control strategies. The study also looked at hospitalisation rates and prevention of thromboembolism.

Methods

SAFIR-RSA was a prospective cross-sectional, non-interventional, observational disease registry carried out in 29 medical institutions spanning nine urban centres in SA. Patients were largely drawn from the private insured medical sector and therefore represent a relatively affluent stratum of the population.

Patients

The study protocol was approved by an independent ethics committee, and written informed consent was obtained from patients before study entry in accordance with Helsinki (1964) ethical recommendations. Adult patients (≥21 years) with electrographically documented AF were enrolled in the registry. Patients were excluded if they had developed AF within 3 months of cardiac surgery, had acute AF apparently precipitated by non-cardiac conditions (e.g. pneumonia), or had recently participated in an AF trial.

Procedure

A medical history taken at enrolment included recording each patient's treatment, the clinical presentation of AF, the presence or absence of comorbidities, and all data pertaining to the primary and secondary outcomes (see below). The physicians or cardiologists in each participating medical centre completed a standardised 6-page case report form for every enrolled patient.

Primary evaluation criteria

These included: (*i*) the prevalence of AF treatment modalities, namely the proportion of patients receiving rhythm control agents (class I and III) and/or rate control agents (class II and IV, and cardiac glycosides), cardioversion, ablation or other procedures; and (*ii*) the use of treatments to prevent thromboembolism, namely the proportion of patients taking vitamin K antagonists, acetylsalicylic acid or other antiplatelet agents. Any other cardiovascular treatments were also noted.

Secondary evaluation criteria

These included: (*i*) the proportion of patients with controlled AF, defined as either in sinus rhythm (SR) (recorded during the visit) or at heart rate control target (≤80 bpm at rest); and (*ii*) the incidence of clinical outcomes in the year preceding the inclusion, defined as hospitalisations for AF and other related cardiovascular events such as stroke, transient ischaemic attack, heart failure and myocardial ischaemia.

Statistical analysis

The data from all the participating medical centres were combined and treated as one dataset for the purposes of the analysis. Data analysis was performed with SAS statistical software, Release 9.2 (SAS Institute, USA). Continuous variables are reported as mean (standard deviation (SD)) and non-continuous variables as number/percentage of patients. The statistical analysis was mainly of a descriptive nature, and sub-analyses were not prespecified in the protocol. Post-hoc sub-analyses were performed using Fisher's exact test. A p-value of <0.05 was considered statistically significant.

Results

The study population consisted of 302 AF patients (59.9% male) from 29 centres, enrolled from 18 February 2010 to 9 March 2011. The mean age was 67 (SD 13) years (range 21 - 95). The mean waist circumference was 101.6 (SD 17.8) cm and the mean body mass index (kg/m^2) 28.8 (SD 5.9), indicating a high prevalence of overweight patients in the cohort.

Clinical characteristics

The single most prevalent clinical characteristic was hypertension (65.9%). Other coronary risk factors were also frequent (dyslipidaemia 48.3% and diabetes 15.6%). Concomitant structural heart disease was common, with 27.5% having valvular disease (of whom 79.5% had mitral valve disease), 26.8% coronary artery disease, and 32.5% heart failure; 28.5% of these patients had New York Heart Association class III or IV symptoms. In keeping with these comorbidities, 27.5% of patients had a history of previous cardiac or vascular interventions. Non-cardiac comorbidities were not common, comprising thyroid disease in 14.2% (3.3% hyperthyroid and 10.9% hypothyroid) and renal disease in 10.9% (Table 1).

The time course of AF was paroxysmal in 32.1% of patients, persistent in 21.2% and permanent in 46.7%. During the preceding 12 months, 40.7% of patients had experienced symptoms of AF.

Pharmacological treatment

The drug therapy at the time of the survey visit is listed in Table 2. For the purposes of this analysis, 'rhythm control' was defined as the chronic use of class Ic or class III drugs for the maintenance of SR, and all others were deemed 'rate control'. Rhythm control was being pursued in 109 patients (36.1%) with class Ic and class III agents, while rate control was pursued in the remainder (63.9%). Amiodarone accounted for 79.4% of class III drugs used. A number of patients in the rhythm control group were receiving rate control medications in addition, but this number is not extractable from the data. Beta-blockers were the most frequently used rate control drugs. Combinations of beta-blockers, digoxin and rate-controlling calcium channel blockers were often employed. Concomitant use of other cardiovascular drugs was high, especially diuretics (53.0%), statins (44.0%), angiotensin-converting enzyme inhibitors (39.1%) and angiotensin receptor blockers (22.5%). For stroke prevention, 75.2% were on warfarin, 39.4% on aspirin and 5.0% on clopidogrel.

Table 1. Clinical characteristics

	History of condition *n* (%)	Treated for condition in preceding 12 months *n* (% of those with condition)
Cardiac risk factors (*N*=302)		
Smoking		
Current	27 (9.0)	
Former	123 (40.7)	
Never	142 (47.0)	
Hypertension	199 (65.9)	198 (99.5)
Diabetes*	47 (15.6)	44 (93.6)
Dyslipidaemia	146 (48.3)	127 (87.0)
Cardiac comorbidities (*N*=302)		
Coronary artery disease	81 (26.8)	23 (28.4)
Myocardial infarction	34 (11.3)	4 (11.8)
Peripheral arterial disease	9 (3.0)	1 (11.1)
Carotid stenosis	3 (1.0)	
Valvular heart disease	83 (27.5)	9 (10.8)
Arrhythmia other than AF†	42 (13.9)	11 (26.2)
Total	83 (27.5)	20 (24.1)
Cardiac and vascular interventions (*N*=83)		
PCI	23 (27.7)	
CABG	16 (19.3)	
Carotid intervention	1 (1.2)	
Valvular surgery	25 (30.1)	
CABG + valvular surgery	3 (3.6)	
PCI + CABG	4 (4.8)	
PCI + valvular surgery	1 (1.2)	
PCI + carotid intervention	1 (1.2)	
Unknown	9 (10.9)	
Non-cardiac comorbidities (*N*=302)		
Thyroid disease	43 (14.2)	
Renal disease	33 (10.9)	

AF = atrial fibrillation; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft.
*97.9% had type 2 diabetes.
†60.4% had atrial flutter.

Events and hospitalisations in the preceding 12 months

Treatments for AF in the preceding 12 months included pharmacological cardioversion (17.5%), electrical cardioversion (13.2%), catheter ablation (4.2%) and pacemaker implantation (5.3%). Interestingly, a number of patients had an unusually large number of cardioversions in the previous year: 6 patients had two attempts at electrical cardioversion, 2 underwent three attempts, and a further 2 underwent four attempts. One patient had six pharmacological cardioversion attempts.

Of the total cohort, 104 patients (34.4%) had required hospitalisation during the previous 12 months, with a third of these patients requiring multiple hospitalisations. AF-related morbidity requiring hospitalisation was particularly frequent for heart failure (11.6% of study patients, 35/98 with heart failure), and for stroke, transient ischaemic attack and peripheral embolism (3.9% of study patients, 12/58 with these conditions) (Table 3). Haemorrhage occurred in 23 patients (7.6%) during the preceding year, but was considered to be serious enough to warrant hospitalisation in only 8 cases. One patient had intracranial haemorrhage. The mean duration of hospital stay was 5.2 days. The average number of outpatient consultations for AF or other cardiovascular reasons in the preceding year was 1.74.

Control of AF

The rhythm status of patients at the time of the survey is shown in Table 4. Only 85 patients (28.1% of the total study cohort) were in SR; notably, 31 of these were on rate control medications alone. Of the patients in AF at the time of the survey, 81.5% were judged in the opinion of the enrolling investigator to be satisfactorily rate controlled. However, when utilising a strict electrocardiogram (ECG) criterion of rate ≤80 bpm, only 58.4% of patients in AF would fulfil this definition. Using the 'lenient' rate control criterion of ≤110 bpm proposed by the RACE II trial,[8] 90.6% of patients would fulfil this definition. 'Therapeutic success' as defined by either the presence of SR or rate-controlled AF was achieved in 86.8% of the total population on the basis of the clinicians' clinical judgement, but only in 70.2% as judged by the EGC criterion of rate ≤80 bpm.

A post-hoc sub-analysis was performed to compare the strategies of rhythm control with rate control (Table 5). Patients prescribed rhythm control medications were somewhat younger, had more medication changes in the preceding year, had more hospitalisations for AF or cardiovascular reasons, and underwent pharmacological and electrical cardioversion more frequently than the rate control group. The rhythm control group had significantly more hospitalisations for coronary artery disease (50.0% v. 16.3%), myocardial infarction (28.6 v. 0%) and heart failure (57.6% v. 25.8%).

Prevention of thromboembolic complications

The mean CHA_2DS_2-VASc score (congestive heart failure or left ventricular dysfunction, hypertension, age ≥75 (2 points), diabetes, stroke (2 points), vascular disease, age 65 - 74, sex category) for the entire cohort of patients was 3.08, and there was no significant difference in scores of patients on warfarin v. those not on warfarin (3.12 v. 2.96, respectively). Of patients not using vitamin K antagonists, 78.6% had CHA_2DS_2-VASc scores ≥2.

There was a poor correlation between the actual CHA_2DS_2-VASc score and use of anticoagulation, as follows: score of 0 (65%); score of 1 (83%); score of 2 (68%); score of 3 (76%); score of 4 (79%); score of 5 (76%); score of 6 (81%); score of 7 (25%, 1/4 patients); score of 8 (100%, 4/4 patients).

Discussion

The primary outcome measure in the SAFIR-RSA survey was to evaluate the incidence of AF treatment modalities and thromboembolic prevention treatments in a cross-sectional

Table 2. Medication at time of visit, *N*=302 patients

Medication	*n* (%)
Cardiovascular	109* (36.1)
Rhythm control agents	
Ic	9 (3.0)
III	102 (33.8)
Rate control agents	
Beta-blockers (excluding sotalol)	180 (59.6)
HR-lowering CCBs	40 (13.2)
Cardiac glycosides	76 (25.2)
Other	
Beta-blockers (not prescribed for AF)	44 (14.6)
Diuretics	160 (53.0)
Dihydropyridine CCBs	43 (14.2)
ACE inhibitors	118 (39.1)
Angiotensin II receptor antagonist	68 (22.5)
Vasodilators	10 (3.3)
Other antihypertensives	19 (6.3)
Statins	133 (44.0)
Other lipid-lowering agents	7 (2.3)
Oral antidiabetic agents	45 (14.9)
Insulin	13 (4.3)
Antithrombotic	
Vitamin K antagonist	227 (75.2)
Acetylsalicylic acid	119 (39.4)
Clopidogrel	15 (5.0)
Other antiplatelet/anticoagulant agents	5 (1.7)
INR in past 6 months	218 (96.0)†

HR = heart rate; CCBs = calcium channel blockers; AF = atrial fibrillation; ACE = angiotensin-converting enzyme; INR = international normalised ratio.
*Two patients were on both class Ic and class III agents.
†75 missing values.

Table 3. AF morbidity in preceding 12 months

Diagnosis	History of condition *n/N* (%)	Hospitalised in preceding 12 months *n* (% of those with condition)
Heart failure (*N*=302)	98 (32.5)	35 (35.7)
NYHA class		
I	22/98 (22.5)	
II	48/98 (49.0)	
III	26/98 (26.5)	
IV	2/98 (2.0)	
LVEF (%) in preceding 12 months (*N*=302)	243 (80.4)	
<30	7/243 (2.9)	
30 - 40	26/243 (10.7)	
41 - 50	33/243 (13.6)	
>50	177/243 (72.8)	
Stroke (*N*=302)	36 (11.9)	3 (8.3)
TIA (*N*=302)	16 (5.3)	7 (43.8)
Peripheral embolic events (*N*=302)	6 (2.0)	2 (33.3)

AF = atrial fibrillation; NYHA = New York Heart Association; LVEF = left ventricular ejection fraction; TIA = transient ischaemic attack.

representative cohort of patients with AF in SA. The results clearly showed that the majority of patients were receiving rate control therapy (63.9%), usually in the form of beta-blockers, either alone or in combination with other rate control agents. Rhythm control therapy for the remainder of the patients consisted primarily of class III agents. Concomitant use of other cardiovascular drugs was high in both treatment strategies. Since the patient cohort included the elderly, with a high frequency of other cardiac risk factors and structural heart disease, it is not surprising that the majority were being treated with a rate control strategy. According to European Society of Cardiology guidelines, rate control is a reasonable strategy in elderly patients in whom the level of symptoms related to AF is deemed acceptable.[8] Nevertheless, the findings do suggest that clinicians in SA apply lenient rate control criteria and judge patients to be rate controlled with a resting pulse rate of less than 110 bpm.

There were no striking differences in the baseline clinical characteristics of this study population when compared with other worldwide registries. Notably, the prevalence of underlying comorbidities such as coronary artery disease, valvular disease and heart failure in the present study is similar (~20 - 30% for each) to those reported in the developed world.[8] This is perhaps not surprising because, although the aim of this study was to focus for the first time on SA patients, the cohort was largely derived (88.7%) from insured patients, a more affluent sector of the population that would more closely approximate a First-World setting. The racial groups of the subjects, frequently used as a proxy for socio-economic status, are unknown.

The primary outcome measure of the SAFIR-RSA survey also included an assessment of the use of thromboembolic prevention treatments. The novel oral anticoagulants were not yet in use at the time of the survey. The findings show that the large majority of patients (75.2%) were receiving warfarin for stroke prevention. There were, however, a significant number of patients not receiving anticoagulation who, with CHA_2DS_2-VASc scores ≥2, should have had thromboembolic prevention therapy according to current treatment guidelines.[10] Nearly all the patients on warfarin had had international normalised ratio monitoring during the previous 6 months. This diligent monitoring may account for the low rate of hospitalisation for haemorrhage of only 2.6% (8 patients) during the preceding year, compared with rates of 6.8 - 7.2% reported in other observational studies on older patients with AF receiving warfarin.[14]

In the present survey, hospitalisations for coronary artery disease, myocardial infarction and heart failure occurred more frequently in the group on antiarrhythmic agents. It is not clear whether these developments are a result of antiarrhythmic drug therapy, or whether rhythm control is preferred as a strategy in patients with these conditions.

Study limitations

There are a number of limitations to this study. The patient sample does not necessarily reflect the true cross-sectional population of AF patients in SA, as most had medical insurance coverage. Site selection bias is likely, with over-representation of cardiologists with specialisation or particular interest in AF. Case selection bias may also have been introduced because it was not mandated that consecutive cases be included at each site. Investigator knowledge of the sponsor

Table 4. Current control at time of the survey

	n (%)	Total patients, *N*
In SR at visit	85 (28.1)	302
In AF at visit	217 (71.9)	
Symptomatic	68 (22.5)	
In AF but rate controlled		
Investigator opinion	177 (81.5)	217
ECG criterion, HR ≤80 bpm	125 (58.4)	214*
ECG criterion, HR ≤110 bpm	194 (90.6)	214*
Therapeutic success (in SR or in AF with rate controlled)		
Investigator opinion	262 (86.8)	302
ECG criteria	210 (70.2)	299*

SR = sinus rhythm; AF = atrial fibrillation; ECG = electrocardiogram; HR = heart rate.
*3 patients in AF did not have ECGs.

Table 5. Sub-analysis of rate control v. rhythm control strategies

	Rate control (*N*=193)	Rhythm control (*N*=109)	*p*-value*
Age (years)	68.3	65.3	0.05
Pharmacological cardioversion, *n* (%)	6 (3.2)	47 (43.9)	<0.001
Electrical cardioversion, *n* (%)	16 (8.4)	24 (22.2)	0.001
AF at visit, *n* (%)	162 (83.9)	55 (50.5)	<0.001
Rate control, *n* (%)	141 (88.1)	36 (65.4)	<0.001
Hospitalisation for AF or CV reasons, *n* (%)†	49 (25.4)	55 (50.5)	<0.001
History of CVD, *n* (%)	51 (27.0)	30 (27.8)	0.892
Hospitalisation for CVD, *n/N* (%)†	8/49 (16.3)	15/30 (50.0)	0.002
History of MI, *n* (%)	20 (10.5)	14 (13.0)	0.57
Hospitalisation for MI, *n/N* (%)†	0 (0)	4/14 (28.6)	0.022
History of CHF, *n* (%)	64 (33.3)	34 (31.2)	0.789
Hospitalisation for CHF, *n* (%)†	16/62 (25.8)	19/33 (57.6)	0.004

AF = atrial fibrillation; CV = cardiovascular; CVD = cardiovascular disease; MI = myocardial infarction; CHF = chronic heart failure.
*Fisher's exact test except for age, where Student's *t*-test was used. Significance values should be interpreted with caution, as the study was not designed for this comparison.
†Preceding 12 months.

may have introduced an additional bias in favour of patients on amiodarone.

Conclusions

The data in the SAFIR-RSA survey conform to similar registries in the developed world. Despite the focus on a relatively affluent sub-sector of the SA population, resulting in a near duplication of studies carried out in other developed countries, this is the first epidemiological study generating data on management of AF in SA. AF is a significant burden in cardiology practice in this country, with considerable resource utilisation and morbidity for patients. This survey highlights a lack of rigour in applying definitions of rate control and under-utilisation of antithrombotic therapy. Although only a 'snapshot', clinicians should be aware of these findings and attempt to improve drug utilisation and patient outcomes.

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