Evaluation of atrial fibrillation (AF) management and cardiovascular risk profile in AF patients: data from Turkish patients in the international observational cross-sectional REALISE AF trial

Atriyum fibrilasyonlu (AF) hastalarda AF yönetimi ve kardiyovasküler risk profilinin değerlendirilmesi: Uluslararası, gözlemsel, kesitsel REALISE AF çalışması Türkiye verileri

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ABSTRACT

Objectives: To assess control of atrial fibrillation (AF) and cardiovascular (CV) risk profile of AF patients with previously established AF therapies.

Study design: A total of 510 patients (mean (SD) age, 67.1 (12.3) years, 55.1% females) enrolled from 40 centers across Turkey were evaluated on a single-visit basis in terms of patient demographics, characteristics of underlying AF, the frequency and scoring of symptoms according to European Heart Rhythm Association AF cardiac symptoms classification, control of AF, cardiovascular (CV) risk profile, AF treatment and the consistency of current therapeutic practice with evidence-based guidelines.

Results: AF was controlled in 39.4% of patients based on sinus rhythm on the day of visit (10.2%) and AF with HR ≤80 bpm (29.2%). Permanent AF was the most commonly identified type of AF (56.0%). Symptoms were evident in 89.2% of patients either before V0 (78.8%) or at V0 (56.5%). Age (72.4%) and hypertension (70.0%) were the leading CV risk factors. Rate-control and rhythm-control strategies were chosen in 76.5 and 19.2% of patients at the enrollment visit. Mean (SD) of EQ-5D scores for VAS and for single index utility were 63.1 (19.8) and 0.62 (0.4), respectively.

Conclusion: In this real life survey of AF patients from Turkey participating in the global contemporary, international, observational, cross-sectional REALISE AF survey, AF was determined to be not optimally controlled, leading patients to experience frequent symptoms, functional impairment and altered QoL,as well as frequent hospital admissions for cardiovascular events and a high requirement for procedures.

ÖZET

Amaç: Atriyum fibrilasyonlu (AF) hastalar AF kontrolü ve kardiyovasküler (KV) risk profili açısından değerlendirildi.

Çalışma planı: Türkiye genelinde 40 merkezden toplam 510 hasta (ort. (SS) yaş: 67.1 (12.3) yıl, %55.1'i kadın) ile tek vizit temelinde gerçekleştirilen bu çalışmada; hastaların demografik özellikleri, AF'nin özellikleri, Avrupa Kalp Ritmi Birliği (EHRA) AF kardiyak semptom sınıflamasına göre semptom sıklığı ve skoru, AF kontrolü, kardiyovasküler (KV) risk profili, AF tedavisi ve uygulanmakta olan tedavi yaklaşımlarının kanıta dayalı kılavuzlarla uyumu değerlendirildi.

Bulgular: Vizit gününde sinüs ritmi (%10.2) veya kalp hızının (KH) ≤80 vuru/dakika (%29.2) olduğu AF şeklinde olmak üzere AF kontrolü hastaların %39.4'ünde mevcuttu. Kalıcı AF (%56.0) en sık gözlenen AF tipi olup, semptomlar V0 öncesi (%78.8) veya V0 esnasında (%56.5) olmak üzere hastaların %89.2'sinde tespit edildi. Yaş (%72.4) ve hipertansyion (%70.0) en önemli KV risk faktörleri olarak saptandı. Hız ve ritm kontrol stratejilerinin kayıt vizitinde hastaların sırasıyla %76.5 ve %19.2'sinde seçildiği belirlendi. Ort. (SS) EQ-5D skorları VAS için 63.1 (19.8) iken yararlanım endeksi için 0.62 (0.4) olarak bulundu.

Sonuç: Uluslararası, gözlemsel, kesitsel ve öncü çalışma niteliğindeki REALISE AF çalışmasına Türkiye'den katılan AF'li hastaların gerçek yaşamdaki tedavi uygulamalarını yansıtan bu çalışmada, AF kontrolünün optimal düzeyde sağlanamadığı ve bu durumun hastalarda semptom sıklığı, fonksiyonel bozukluk ve yaşam kalitesi değişimlerinin yanı sıra KV olaylar nedeni ile hastanaye başvuru ve müdahale gereksiniminde artışa yol açtığı tespit edilmiştir.

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As the most common and sustained cardiac arrhythmia associated with a significant burden on patients and the health care system, atrial fibrillation (AF) is a supraventricular arrhythmia characterized by uncoordinated atrial activation, with consequent loss of atrial mechanical function.[1,2]

While the exact incidence and prevalence in the general population are unknown because of its often asymptomatic course,[3] an estimated 2.3 million people in North America and 4.5 million people in the European Union have AF.[4]

In a prospective, cross-sectional study on the incidence, prevalence, and mortality estimates for chronic atrial fibrillation in Turkish adults (TEKHARF Study) conducted among 3.450 (1707 men, 1743 women; mean age 52±13 years) patients who were surveyed until 2006/07, the current incidence and prevalence of chronic AF was estimated to be 35.000 per year (22.000 in women) and 310.000 (200.000 in women) respectively.[5]

The main goals of atrial fibrillation therapy are to improve symptoms, reduce morbidity (stroke, heart failure) and possibly reduce, or at least not increase, mortality.[2]

Randomized clinical trials (RCTs) that have compared rate- and rhythm-control strategies, including The Atrial Fibrillation Follow up Investigation of Rhythm Management (AFFIRM), Rate Control Versus Electrical Cardioversion for Persistent Atrial Fibrillation (RACE), Pharmacological Intervention in Atrial Fibrillation (PIAF), and Strategies of Treatment of Atrial Fibrillation (STAF), have demonstrated no difference in mortality between rate- and rhythm-control strategies.[6-9] In the first worldwide prospective, 1-year observational study on the real life management of paroxysmal/persistent AF in recently diagnosed patients, the RecordAF study confirmed that recently- diagnosed and actively-treated AF patients, within a short one year period, suffer from a high rate of clinical events (18%), the majority (90%) of which were cardiovascular (CV) hospitalizations. Furthermore, while the superiority of rhythm-control strategy was shown in short-term control of arrhythmia, no difference was reported between rate- and rhythm-control strategies in terms of clinical events.[10]

Based on unsatisfactory results with current AF treatment strategies, the RecordAF results stress the need for newer antiarrhythmic agents able to successfully achieve rhythm-control, rate-control or both, and more importantly, able to decrease clinical events in order to optimize comprehensive management of AF patients.[10]

Abbreviations:

AAD	*Antiarrhythmic drug*
ACC	*American College of Cardiology*
AF	*Atrial fibrillation*
AHA	*American Heart Association*
BMI	*Body mass index*
CAD	*Coronary artery disease*
CV	*Cardiovascular*
ESC	*European Society of Cardiology*
LV	*Left ventricular*
QoL	*Quality of Life*
REALISE AF	*Real life global survey evaluating patients with atrial fibrillation*
SD	*Standard deviation*

Although RecordAF contradicts the common view on equipotency of rate-control and rhythm control in AF management, lack of similar evidence concerning the superiority of rhythm-control in reduction of clinical events led to the therapeutic success in AF being redefined, considering the multifaceted impact of AF. Moreover, RecordAF was designed as a prospective cohort study including patients with paroxysmal and persistent AF only, for less than one year, and thus represented a limited spectrum of all AF patient types. Accordingly, the conduction of a new international observational study concerning CV risk profiles, ongoing treatment strategies and related outcomes in real life clinical practice of AF management in all AF types and without time limitation in disease history has become an absolute requisite.

In this respect, based on the crucial role of understanding the epidemiology and natural history of AF in the future allocation of resources and utilization of an expanding range of therapies,[11] and the need for contemporary, international, representative information on patients characteristics and management of patients with the whole spectrum of AF, the present study, which constitutes the Turkish part of the multinational cross-sectional REALISE AF (Real life global survey evaluating patients with atrial fibrillation) conducted across 26 countries, was designed to assess patient profile and control of AF (either in SR or in AF with HR ≤80 bpm) with previously-established AF therapies, and to investigate the CV risk profile of AF patients.[12]

PATIENTS AND METHODS

Study population

Of the total population of 10.523 patients across 26 countries in the cross-sectional observational RE-

ALISE AF study, 513 Turkish AF patients were enrolled from 40 centers. Patients were selected via random sampling method from among hospitals across Turkey and evaluated by randomly selected cardiologists and internists, the ratio of which was pre-determined on a national basis from existing data.

Of the total patients enrolled from Turkey, 510 were considered eligible in terms of history of AF (treated or not and whatever the rhythm at inclusion), with at least one AF episode documented by standard ECG or by ECG-Holter monitoring in the previous 12 months, or documented current AF. 3 patients were excluded due to lack of history of AF (n=1) and other reasons (n=2). Inability to provide consent, having post-operative AF (<3 months after surgery) and participation in an AF or antithrombotic clinical trial in the previous month were the exclusion criteria of the study.

Data collection was performed during Nov-Dec 2009 at a single time point during the enrollment, which was planned to be short (<6 weeks) to maximize consecutive recruitment.

Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study. The study was conducted in accordance with the Helsinki Declaration, and approved by the institutional ethics committee.

Data collection

Data on patient demographics (age, gender), anthropometric measurements (weight, height, body mass index (BMI), and vital signs (systolic and diastolic blood pressure) were recorded. Characteristics of underlying AF [family history for the disease, time since initial diagnosis, timing of episode confirmed within the last 12 months via standard ECG or ECG-Holter, type of AF (paroxysmal, persistent, permanent, or unable to assign-first episode), etiology of AF (primary factors, precipitating factors, unknown), the frequency of patients with pre-specified symptoms and the scoring of symptoms according to EHRA AF cardiac symptoms classification] and control of AF (defined by being in sinus rhythm assessed by at rest ECG on the day of the visit or in AF with at rest heart rate ≤80 beats/minute) were determined. Data on CV risk profile (risk factors, comorbidities) of AF patients, ECG-based diagnosis of left ventricular hypertrophy, anticoagulant treatment, AF treatment (rate and/or rhythm control management strategies, antiarrhythmic agents, cardioversion, ablation, device implantation, antithrombotic agents), consistency of the current therapeutic practice with evidence based guidelines, definition of cardiovascular events leading to hospitalization within the previous 12 months, cardiovascular interventions without a specific relation to AF in the same time period, and Health-related Quality of Life (QoL) associated with AF were also collected during enrollment. Family history of premature cardiovascular disease, smoking status, obesity, arterial hypertension, diabetes mellitus and dyslipidemia were the recorded cardiovascular risk factors. Additionally, data was collected at each center on demographics, specialty (cardiology/internal medicine), years of work, hospital type and the number of patients with current AF, new onset AF and history of AF seen per week.

In light of the American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) guidelines, patients with AF were detected on the basis of clinical history documentation and electrocardiographic evidence, and classified as paroxysmal, persistent, or permanent. Paroxysmal pattern was considered in patients with documented AF who have spontaneous restoration of sinus rhythm. Patients with sustained AF who typically (although not always) require cardioversion to reestablish the sinus rhythm were considered to have persistent pattern, while the permanent pattern was considered in patients who have AF on serial electrocardiograms without evidence of interval sinus rhythm, whether or not cardioversion has been attempted.[13]

Statistical analysis

Assuming the percentage of patients achieving AF control to be around 50% while that of non-evaluable patients to be 10%, inclusion of 400-900 patients per country or region with 3.5-5% error within 95% confidence interval (CI), the sample size was calculated to be minimum 10.000 patients. Accordingly, 510 patients were included from Turkey in accordance with the patient number calculated per country.

Statistical analysis was made using SAS® statistical software, Version 9.2 (SAS Institute, Cary, NC, USA). Population characteristics were summarized as mean (Standard deviation [SD]) for continuous variables and count (percentage) for qualitative variables, unless otherwise indicated. Descriptive analyses were conducted on the total population.

RESULTS

Patient demographics and basic clinical features (Table 1)

Our study population was composed of 510 patients (55.1% females; 93.7% Caucasian) having mean (SD) age of 67.1 (12.3) years. 31.8% were determined to be ≥75 years of age. Mean (SD) BMI (kg/m^2) was determined to be 28.4 (5.2) while obesity (BMI ≥30 kg/m^2) was evident in 32.9% (n=168) of the population. Mean (SD) systolic/diastolic blood pressure level was 129.5 (20.7)/78.9 (12.0) mmHg. Blood pressure was controlled in 52.3% of patients. The percentages of inpatients and outpatients were 36.1% (n=184) and 63.9% (n=326) respectively. At least one comorbid disorder was identified in 80.8% of patients. Administration of oral anticoagulant therapy in the form of Vitamin K antagonist (warfarin) in all patients was noted in 40.4% of patients.

Considering cardiovascular risk profile, current smoking (9.0%), diabetes mellitus (24.3%), arterial hypertension (70.0%), dyslipidemia (33.1%) and family history of premature cardiovascular disease (25.8%) were the identified risk factors (Table 1).

Cardiovascular history revealed heart failure (43.8%) with current NYHA class II identified in 22.1% of patients, coronary artery disease (33.3%), peripheral arterial disease (2.4%), cerebrovascular disease (13.0%), valvular heart disease (41.7%), carotid stenosis ≥50% (2.6%) and venous thromboembolism (2.3%) (Table 1).

Control and baseline characteristics of AF

AF was determined to be controlled in 39.4% of patients based on being in sinus rhythm the day of visit (10.2%) or in AF with HR ≤80 bpm (29.2%) (Table 2).

In 55.8% of patients, AF had been evident for more than 12 months, with mean (SD) duration of disease determined to be 40.1 (61.4) months. The most commonly identified AF types were permanent (56.0%) and persistent (20.7%) followed by paroxysmal (12.6%) AF. Lone AF, defined as being aged <60 years with no coronary artery disease (CAD), heart failure, valvular heart disease, chronic pulmonary disease, VTE or arterial hypertension was identified in 4.3% of patients, lone AF or hypertension without left ventricular (LV) hypertrophy in 66.5%, heart failure

Table 1. Demographical and basic clinical characteristics of patients (n=510)

	n	%
Age years; mean (SD)	67.1	12.3
<75 years	348	68.2
≥75 years	162	31.8
Gender		
Male	229	44.9
Female	281	55.1
Body Mass Index (kg/m^2)	28.4	5.2
Blood pressure control[a]	266	52.3
Obesity (BMI ≥30 kg/m^2)	168	32.9
Comorbidities		
Chronic pulmonary diseases	80	16.0
Thyroid diseases	42	8.5
Hypothyroidism	18	3.7
Hyperthyroidism	24	4.9
Liver diseases	6	1.2
Chronic advanced renal failure	15	3.0
Malignancies	13	2.6
≥1 comorbidity	401	80.8
Risk factors		
Older age (>50 for males, >65 for females)	369	72.4
Current smoking	46	9.0
Diabetes	123	24.3
Hypertension	354	70.0
Dyslipidemia	487	33.1
Family history of premature cardiovascular disease	116	25.8
Cardiovascular history		
Heart failure	221	43.8
Current NYHA class		
1	29	5.8
2	111	22.1
3	58	11.6
4	19	3.8
Coronary artery disease	151	33.3
Peripheral artery disease	11	2.4
Cerebrovascular disease	65	13.0
Valvular heart disease	210	41.7
Carotid stenosis ≥50%	11	2.6
Venous thromboembolism	11	2.3
At least one oral anticoagulant agent in the previous 7 days	206	40.4
Vitamin K antagonist (Warfarin)	206	40.4
Other oral anticoagulant agents	0	0.0

[a]Blood pressure was considered to be controlled for SBP ≥130 mmHg or DBP ≥80 mmHg in diabetic patients and SBP ≥140 mmHg or DBP ≥90 mmHg in non-diabetic patients.

Table 2. Control and basic characteristics of AF (n=510)

	n	%
AF controlled	201	39.4
Sinus rhythm on the day of the visit	52	10.2
AF with HR ≤80 bpm	149	29.2
AF not controlled	299	58.6
(AF with HR >80 bpm)		
Not evaluablea	10	2.0
Family history of AF	46	9.0
Time since initial AF diagnosis in months (mean[SD])	40.1	61.4
<3 months	134	26.4
3 to 6 months	25	4.9
6 to 12 months	65	12.8
>12 months	283	55.8
Missing	3	
Lone AF[b]	22	4.3
Lone AF or hypertension without LV hypertrophy	336	66.5
Heart failure or hypertension with significant LV hypertrophy	240	47.7
Lone AF or hypertension without LV hypertrophy or CAD	386	78.8
Type of AF		
Paroxysmal	64	12.6
Persistent	105	20.7
Permanent	284	56.0
Unable to assign (first episode)	53	10.5
Etiology		
Missing	194	
Primary	257	81.3
Precipitating factors	59	18.7
Thyrotoxicosis	12	3.8
Alcohol intoxication	5	1.6
Hydroelectrolytic disorders	5	1.6
Infection/Fever	4	1.3
Hypoxia/Respiratory failure	24	7.6
Exercise	18	5.7
Vagal	1	0.3

[a]Control of atrial fibrillation was not evaluable in patients lacking ECG or missing data on sinus, AF or heart rate; [b]Defined in patients aged under 60 years with no coronary artery disease, heart failure, valvular heart disease, chronic pulmonary disease, VTE or arterial hypertension.

or hypertension with significant LV hypertrophy in 47.7% and lone AF or hypertension without LV hypertrophy or CAD in 78.8% of patients (Table 2).

Primary etiology was evident in 81.3% of patients while the precipitating factors were evident in 18.7%. Hypoxia/respiratory failure (7.6%) and exercise (5.7%) were the leading precipitating factors (Table 2).

Symptom profile (at the time of visit, in the previous 7 days and in the past 12 months) and cardiovascular events and interventions in the previous 12 months.

At the time of visit, 52.0% of patients were identified to be class II according to EHRA AF Cardiac Symptoms classification. When symptoms occurring in the week leading to and including the day of visit were considered, dyspnea (34.5%), palpitations (34.3%), and fatigue (32.5%) were the most commonly identified symptoms (Table 3).

The most commonly identified AF symptoms in the year leading up to the day of visit, but excluding the week immediately before the visit, were palpitations (59.4%), dyspnea (55.7%) and fatigue (43.7%) (Table 3).

Considering CV events leading to hospitalization, and CV interventions performed within the previous 12 months, at least one cardiovascular event excluding major bleeding was evident in 33.4% of the patient population, while acute decompensation of heart failure (16.4%) and stroke (10.4%) were the most commonly identified events (Table 3).

Patients with at least one cardiovascular intervention composed 22.2% of the population, while percutaneous coronary intervention (10.0%) and valvular surgery (9.0%) were identified as the most common interventions (Table 3).

According to ECG findings on the visit day, 88.4% of patients were in atrial fibrillation, 0.4% in atrial flutter, and 10.3% in sinus rhythm.

AF Management: rhythm vs. rate control strategy

While identified as being administered in 69.6% and 15.3% of patients before the enrollment visit, rate- and rhythm-control strategies were chosen in 76.5% and 19.2% of patients at the enrollment visit. The percentage of patients treated with rhythm control strategy before and after visit 0 was 83.3%, while 95.8%

Table 3. Symptom profile and cardiovascular events and interventions

	n	%
Symptoms at the time of visit (EHRA score)		
I	122	23.9
II	265	52.0
III	103	20.2
IV	20	3.9
≥1 symptom within the past 12 months	455	89.2
Symptoms in the previous 7 days		
≥1 symptom	288	56.5
Palpitations	175	34.3
Dyspnea	176	34.5
Fatigue	166	32.5
Lightheadedness/dizziness	69	13.5
Chest pain	67	13.1
Syncope	15	2.9
Symptoms in the past 12 months (excluding previous 7 days)		
≥1 symptom	402	78.8
Palpitations	303	59.4
Dyspnea	284	55.7
Fatigue	223	43.7
Lightheadedness/dizziness	122	23.9
Chest pain	119	23.3
Syncope	17	3.3
Cardiovascular events leading to hospitalization in the past 12 months		
Acute coronary syndrome	45	9.0
Stroke	53	10.4
Transient ischemic attack	18	3.6
At least one arrhythmic or proarrhythmic event	35	7.1
Supraventricular tachycardia	21	4.2
Atrial flutter 1 to 1	1	0.2
Ventricular tachycardia	4	0.8
Ventricular fibrillation/Resuscitated cardiac arrest	1	0.2
Clinically significant bradycardia/ AV block	11	2.2
Acute decompensation of heart failure	83	16.4
Non CNS peripheral embolic events	4	0.8
Pulmonary embolism	7	1.4
At least one major bleeding	10	2.0
Symptomatic bleeding in a critical area or organ	4	0.8
Bleeding causing a decrease of haemoglobin	8	1.6
Bleeding leading to transfusion	7	1.4
≥1 event (excluding major bleeding)	167	33.4
ECG on day of visit		
Atrial fibrillation[a]	448	88.4
Atrial flutter[b]	2	0.4
Sinus rhythm[c]	52	10.3
Cardiovascular interventions in the past 12 months		
Percutaneous coronary intervention	51	10.0
Coronary artery bypass graft	24	4.7
Valvular surgery	46	9.0
Carotid angioplasty or endarterectomy	2	0.4
Other CV surgical intervention	9	1.8
≥1 intervention	113	22.2

Missing data in 3[a], 1[b,d,j], 5[c,f], 7[e], 2[g], 458[h], 4[i] patients.

Table 4. AF Management in relation to rhythm-control and rate control strategies applied before and after the enrollment visit

	Strategy before visit 0							
	Rhythm control		Rate control		None		Total	
	n	%	n	%	n	%	n	%
Strategy at visit 0								
Rhythm-control	65	83.3	15	4.2	18	23.4	98	19.2
Rate-control	11	14.1	340	95.8	39	50.6	390	76.5
None	2	2.6	0	0.0	20	26.0	22	4.3
Total	78	15.3	355	69.6	77	15.1	510	100.0

of patients were treated with rate control strategy both before and after visit 0. During the enrollment visit, 14.1% of patients on rhythm-control strategy were switched to rate-control strategy while 4.2% of patients on rate-control strategy were switched to rhythm-control strategy (Table 4).

AF Management: antiarrhythmic drugs (AADs)

At least one AAD was administered in 84.9% of patients before the enrollment visit and in 67.8% of patients at the enrollment visit. AAD class II agents were the most commonly prescribed drugs in 51.8% before the enrollment visit and in 44.1% of patients at the enrollment visit, respectively. Change in the class of AAD was present in 3.9% of patients, while addition and discontinuation of AAD at the enrollment visit were identified in 14.1% and 26.3% of patients, respectively (Table 5).

AF Management according to types of AF

In patients with paroxysmal or persistent AF (n=169), amiodarone as a first line therapy was prescribed in 24 (14.2%) patients at visit 0, and 50% (n=12) of these patients had heart failure or hypertension with significant LV hypertrophy (Table 6).

In patients with permanent AF (n=284), at least one cardiac glycoside was recorded at visit 0 in 35.9% of patients, at least one AAD class II for reasons of AF in 33.1%, while patients without Class II and IV AADs or digoxin composed 41.9% of the population. Class II AAD (15.1%), digoxin (14.1%) and Class II AAD+digoxin combination (12.3%) were the most commonly prescribed agents at visit 0 in patients with permanent AF (Table 6).

In 37.7% of patients lacking assignment of AF type since they had had the first AF episode, no AAD was initiated at visit 0 while administration of at least one AAD class II (28.3%), cardiac glycosides (22.6) and AAD class III (13.2) were the most commonly-selected therapeutic options (Table 6).

Management of AF: impact of co-morbidities

Rate control was more commonly selected in each comorbid disorder. In patients with no comorbidities, rhythm control was more common in patients with 0-1 (100.0 and 70.0%, respectively) CV risk factor, but rate control was more common in patients with higher number of risk factors (63.2% and 62.5%, respectively) (Table 7).

QoL based on EQ5D questionnaire

According to the EQ5D questionnaire, mean (SD) of EQ-5D scores for VAS and for single index utility were determined to be 63.1 (19.8) and 0.62 (0.4), respectively (Table 8).

DISCUSSION

In this sub-group of 510 Turkish patients from the real life survey, the results are in line with global data.[12] AF was determined to be not optimally controlled, frequently associated with co-morbidities, multiple CV risk factors, CV events requiring hospitalization and major CV interventions, while patients had a high symptom burden and disturbed QoL.

As to types of AF, the permanent type was dominant (56.0%) in the Turkish population while the paroxysmal type was less frequent (12.6 *vs.* 24.8%),

Table 5. AF Management in terms of anti-arrhythmic drugs in the last week and at the enrolment visit

	Last week		Enrollment visit	
	n	%	n	%
At least one AAD	433	84.9	346	67.8
AAD class Ia	0	0.0	3	0.6
Quinidine	0	0.0	0	0.0
Procainamide	0	0.0	0	0.0
Disopyramide	0	0.0	3	0.6
Other class Ia	0	0.0	0	0.0
AAD class Ic	22	4.3	15	2.9
Flecainide	0	0.0	0	0.0
Propafenone	21	4.1	15	2.9
Other class Ic	1	0.2	0	0.0
AAD class II	264	51.8	225	44.1
Missing	2		1	
Beta blockers for AF reason	197	38.8	178	35.0
Beta blockers for Non AF reason	115	22.6	98	19.3
AAD class III	44	8.6	55	10.8
Dofetilide	0	0.0	0	0.0
Amiodarone	42	8.2	53	10.4
Amiodarone in 2nd line	8	1.6	7	1.4
Sotalol	2	0.4	2	0.4
Dronedarone	0	0.0	0	0.0
Other class III	0	0.0	0	0.0
AAD class IV	132	25.9	81	15.9
CCB for AF reason	96	18.8	61	12.0
CCB for Non AF reason	57	11.2	37	7.3
At least one Cardiac glycosides in the previous 7 days	195	38.2	165	32.4
Change* of AAD class between before V0 and at V0		n	%	
No Change		224	43.9	
No AAD before V0 and AAD at V0		72	14.1	
Change of class		20	3.9	
AAD before V0 and no AAD at V0		134	26.3	
Any additional/discontinued class		60	11.8	

*No change= same class(es) of AF treatment before and at V0. Regarding change involving class II or IV, only Class II or IV prescribed for AF reason have been taken into account.

and having the first episode of AF was more common (10.5% *vs.* 6.4%) than in global REALISE AF data.[12]

In line with global data[12] and in relation to insufficient AF control, CV events leading to unplanned hospitalization in AF patients included in the present study were frequent and severe. Experience of at least one cardiovascular event (excluding major bleeding) leading to hospitalization in the past 12 months was slightly more common compared with global findings (33.4% *vs.* 28.1%), while acute decompensation of heart failure (16.4%) and stroke (10.4%) were the leading events.

Table 6. Management of AF with respect to type of AF at enrolment visit

	n	%
Patient with a paroxysmal or persistent AF (n=169)		
At least one AAD class Ic at V0	14	8.3
Lone AF or hypertension without LV hypertrophy	13	92.9
Other	1	7.1
Amiodarone in 1st line prescribed at V0	24	14.2
Heart failure or hypertension with significant LV hypertrophy	12	50.0
Other	12	50.0
Amiodarone in 2nd line prescribed at V0	4	2.4
Lone AF or hypertension without LV hypertrophy or CAD	3	75.0
Other	1	25.0
Sotalol, prescription at V0 (day of the visit)	1	0.6
Lone AF or hypertension without LV hypertrophy or CAD	0	0.0
Other	1	100
Patients with permanent AF (n=284)		
At least one AAD class II for AF reason at V0	94	33.1
At least one AAD class IV for AF reason at V0	34	12.0
At least one cardiac glycosides at V0	102	35.9
Patients without Class II and IV agents or Digoxin	119	41.9
Association of AAD at V0*		
Class I	1	0.4
Class I + Digoxin	2	0.7
Class II	43	15.1
Class II + Class III	4	1.4
Class II + Class III + Digoxin	2	0.7
Class II + Class IV	6	2.1
Class II + Class IV + Digoxin	4	1.4
Class II + Digoxin	35	12.3
Class III	6	2.1
Class III + Class IV + Digoxin	1	0.4
Class III + Digoxin	5	1.8
Class IV	10	3.5
Class IV + Digoxin	13	4.6
Digoxin	40	14.1
No AAD	112	39.4
Patients with unassigned AF type due to first episode		
No AAD treatment at V0	20	37.7
At least one AAD class I at V0	0	0.0
At least one AAD class II at V0 for AF reason	15	28.3
At least one AAD class III at V0	7	13.2
At least one AAD class IV at V0 for AF reason	6	11.3
At least one cardiac glycosides at V0	12	22.6

*For the association at V0, only Class II or IV prescribed for AF reason have been taken into account.

Table 7. Management of AF with respect to impact of comorbidities

Therapeutic strategy chosen at V0	Heart Failure			Total
	No HF or HF class I (n=312)	HF class II (n=111)	HF class III or IV (n=77)	n=500
Rhythm-control	82 (26.3)	6 (5.4)	6 (7.8)	94 (18.8)
Rate-control	213 (68.3)	103 (92.8)	68 (88.3)	384 (76.8)
None	17 (5.4)	2 (1.8)	3 (3.9)	22 (4.4)
	Coronary artery disease			Total
	Yes (n=151)	No (n=303)		(n=454)
Rhythm-control	23 (15.2)	72 (23.8)		95 (20.9)
Rate-control	119 (78.8)	220 (72.6)		339 (74.7)
None	9 (6.0)	11 (3.6)		20 (4.4)
	Peripheral arterial disease			Total
	Yes (n=11)	No (n=448)		(n=459)
Rhythm-control	2 (18.2)	93 (20.8)		95 (20.7)
Rate-control	9 (81.8)	334 (74.6)		343 (74.7)
None	0 (0.0)	21 (4.7)		21 (4.6)
	Cerebro-vascular disease			Total
	Yes (n=65)	No (n=434)		(n=499)
Rhythm-control	10 (15.4)	88 (20.3)		98 (19.6)
Rate-control	50 (76.9)	330 (76.0)		380 (76.2)
None	5 (7.7)	16 (3.7)		21 (4.2)
	Valvular heart disease			Total
	Yes (n=210)	No (n=294)		(n=504)
Rhythm-control	22 (10.5)	74 (25.2)		96 (19.0)
Rate-control	182 (86.7)	204 (69.4)		386 (76.6)
None	6 (2.9)	16 (5.4)		22 (4.4)
	No comorbidities (number of CV risk factors in classes)			Total
	Missing (n=1)	0 (n=2)	1 (n=10)	2 (n=19)	>=3 (n=64)	(n=96)
Rhythm-control	0 (0.0)	2 (100)	7 (70.0)	7 (36.8)	22 (34.4)	38 (39.6)
Rate-control	1 (100)	0 (0.0)	3 (30.0)	12 (63.2)	40 (62.5)	56 (58.3)
None	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.1)	2 (2.1)

In relation to poor AF control, at least one symptom was evident in the majority of our population, this despite the cross-sectional design of the study, with enrollment of patients regardless of their status and treatment expected to minimize skewing towards selection of highly symptomatic patients observed in past studies of rate- or rhythm-control.[14]

Accordingly, a high symptom frequency has already been seen in other registries: in the EuroHeart Survey on AF,[15] 69% of patients were symptomatic at the time of the survey. Likewise, in a Swiss office-based survey,[16] 73.8% of patients with AF had symptoms, a figure consistent with the 89.2% observed in our report, as well as global report (73.9%).[12] Oc-

Table 8. QoL with repsect to five dimensions of well-being and scores obtained from EQ5D questionnaire

EQ-5D- Five dimensions of well-being	n	%
Mobility		
Missing	52	
I have no problems in walking about	154	33.6
I have some problems in walking about	286	62.4
I am confined to bed	18	3.9
Self-care		
Missing	53	
I have no problems with self-care	282	61.7
I have some problems washing or dressing myself	146	31.9
I am unable to wash or dress myself	29	6.3
Usual activities		
Missing	53	
I have no problems with performing my usual activities	213	46.6
I have some problems with performing my usual activities	194	42.5
I am unable to perform my usual activities	50	10.9
Pain/Discomfort		
Missing	53	
I have no pain or discomfort	208	45.5
I have moderate pain or discomfort	217	47.5
I have extreme pain or discomfort	32	7.0
Anxiety/Depression		
Missing	51	
I am not anxious or depressed	212	46.2
I am moderately anxious or depressed	205	44.7
I am extremely anxious or depressed	42	9.2
EQ-5D Scores		
VAS (Your own health state today)	63.1	19.8
Single index utility	0.62	0.4

VAS: Visual Analogue Scale.

curring independent of the known predisposing conditions, doubling in the prevalence of AF with each decade of age is associated age-related cardiac abnormalities as well as increased vulnerability due to longer exposure to predisposing conditions for AF.[17,18]

Rate control was the most commonly selected strategy in the overall population in the present study, regardless of the type of comorbid disorders, while in patients with no co-morbidities rhythm control was more common in patients with risk factor number of 0-1 (100.0 and 70.0%, respectively) but rate control more common in patients with higher number of risk factors (63.2 and 62.5%, respectively). Rhythm control strategy was lower than reported globally (19.0% vs. 37.2%), while rate control was determined to be selected more commonly (76.5% *vs.* 57.5%) when compared to overall data obtained in global analysis of AF patients from all countries.[12]

In the management of paroxysmal and persistent AF, the prescription of at least one class Ic AAD in 8.3% of patients was similar to global data (6.5%). In permanent AF, class II AADs (33.1%), cardiac gly-

cosides (35.9%) and class IV AADs (12.0%) were the most commonly selected regimens, while patients without AAD or digoxin administration composed 41.9% of the population. In our patients with first episode, no AAD was prescribed at enrollment visit in 37.7% of patients while, class II AADs (28.3%) and cardiac glycosides (22.6%) were the common selections. At least one AAD was prescribed in 67.8% of patients at visit 0, with class II (44.1%), class IV (15.9%), class III (10.8%; amiodarone as a first line in 10.4%, as a second line with sotatol in 0.4%) and class Ic (2.9%; only propafenone) agents. Use of amiodarone as a first or second line drug was lower in Turkey compared with global data (16.6% vs. 22.3%).[12]

The basic and interrelated aims of AF treatment have been considered as rate control, prevention of thromboemboli and correction of rhythm disorder. In this respect, selection of one of the rate or rhythm control strategies has priority in the management of the disease, with recommended inclusion of antithrombotic treatment to prevent thromboembolic complications, regardless of the chosen strategy.[19]

Treatment guidelines by the ACC/AHA/ESC 2006 task force[13] indicate the debate on therapeutic management of AF due to lack of safe and efficient antiarrhythmic agents available. While prior strategies focused on restoration and maintenance of sinus rhythm,[13] the current approach is based on rate control and anticoagulation, reserving rhythm control for symptomatic patients.[15]

However, two strategies were documented as similar in terms of long-term outcome in recent randomized clinical trials, while data on the importance of anticoagulation in patients with high risk for stroke development are consistent, regardless of the selected anti-arrhythmic strategy.[15,20] Besides, while the impact of thromboprophylaxis on morbidity and mortality was confirmed, there is no evidence on such an effect of either rate or rhythm control strategies.[21]

Owing to the variety of clinical presentations and treatment options for AF, heterogeneity in 'real-life' management of AF is expected, and despite the availability since 2001 of ACC/AHA/ESC guidelines for AF management, it remains unclear how well clinicians adhere to them.[22,23]

Providing a unique snapshot of the characteristics and management of AF patients in cardiology departments among ESC member countries, the Euro Heart Survey on Atrial Fibrillation indicated that, in fair agreement with the guidelines, 67% of currently symptomatic patients received a rhythm control strategy.[23] However given that available rhythm control strategies are inadequate and that there is at present an unmet need for safe and efficacious anti-arrhythmic drugs for control of A, most rhythm-controlled patients were reported as suffering from arrhythmia symptoms rather than complaints due to associated cardiac disease.[23]

On the other hand, rhythm control was reported as applied in 44% of cases despite the absence of AF symptoms, while rate control to prevent late onset heart failure is probably sufficient, and may also help to avoid possible adverse effects of rhythm control. The ACC/AHA/ESC guidelines in 2006[19] and ESC guideline in 2010[22] state that rhythm control should be applied only in symptomatic patients, as supported by the findings from the large rate vs. rhythm trials which showed that compared to existing rhythm control strategies, rate control seems safer and as effective as rhythm control.[7,8,15]

The recently published RecordAF (REgistry on Cardiac rhythm disORDers) study including a total of 5.895 patients with paroxysmal or persistent AF from 21 countries indicated that rate control strategy was more common in the USA than other parts of the world, and higher use of rate control among persistent AF patients than paroxysmal AF patients in relation to increased cardiovascular risk.[10]

Despite the many technological advances that have been made in the treatment of AF over the past 2 decades, including ablation and use of anti-tachycardia devices, little is known about long-term outcomes in terms of survival and quality of life. In addition, more recent studies have shown that survival did not differ between rate- and rhythm-control strategies.[24] In agreement with these studies, preliminary data from an Olmsted County Study showed a disappointing lack of overall improvement in survival for the period 1980 to 2000, despite all the technological and pharmacological innovations that came into clinical use over this time.[25]

Further, it has been recommended that instead of focusing on solely the electrocardiographic results and considering "rhythm versus rate control", one

needs to consider "symptom control" as well as patient well-being. Given that these three components are related and overlapping but not identical, the success or failure of therapy should not be judged by the electrocardiographic result alone, but rather by the symptoms and well-being of the patient.[26]

In this context, since the results of several studies that have compared rate- and rhythm-control strategies in AF[6,27-30] have not indicated a clear superiority of rhythm-control compared with rate control strategies, even in patients with heart failure,[31] both strategies are considered acceptable for the management of patients with AF. Nevertheless, our findings provide information about how frequently restoration and maintenance of sinus rhythm or adequate control of AF rate are achieved in a sample of patients with AF, representative of routine practice in Turkey.[12]

Improvement of quality of life of AF patients is a therapeutic goal in the new 2010 ESC guidelines,[22] while current AF management doesn't necessarily achieve this objective. Based on similar mean (SD) of EQ-5D scores for VAS (63.1 [19.8]) and for single index utility (0.62 [0.4]) with global data in our study population, both high symptom burden and disturbed QoL seem to be evident despite modest improvement in well-being. Thus, the enormous burden of AF shown by symptoms, QoL, cardiovascular events, hospitalizations, procedures and their attendant costs were reported to emphasize the need for improved treatments for this increasingly common condition.[12]

Accordingly, REALISE AF encloses a much larger population of AF patients than the RecordAF study, due to lack of AF type and duration-based limitations on patient inclusion, and evaluates not only rate vs. rhythm control strategies but also patient profiles, control of the disease and CV risk profile. In this regard, REALISE AF is the first international cross-sectional large-scale study contributing to the data on epidemiological and clinical features as well as therapeutic management in relation to available guidelines among AF patients, with a contemporary, international, representative source of information on patients across the whole spectrum of AF.

In conclusion, in this real life sub-group of the REALISE AF survey encompassing 510 Turkish AF patients in the global contemporary, international, observational, cross sectional REALISE AF survey, AF was determined to be not optimally-controlled, leading patients to experience frequent symptoms, functional impairment and altered QoL, as well as frequent hospital admissions for cardiovascular events and a high requirement for procedures. In this respect, our findings highlight the need for improved treatments in the management of AF to increase control of the disease, reduce symptoms, minimize functional impairment and improve QoL.

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Key words: Atrial fibrillation; patient care management; cardiovascular diseases; guidelines as topic; Turkey.

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