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CLINICAL RESEARCH
Arrhythmia/electrophysiology

Autonomic trigger patterns and anti-arrhythmic treatment of paroxysmal atrial fibrillation: data from the Euro Heart Survey

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Aims To investigate the clinical characteristics, management, and outcome of patients with paroxysmal atrial fibrillation (AF) associated with autonomic triggers.

Methods and results One thousand five hundred and seventeen patients with paroxysmal AF participated in the Euro Heart Survey on AF. We categorized patients according to trigger pattern as reported by the physician: adrenergic (AF associated with exercise, emotion or during daytime only and absence of vagal triggers), vagal (postprandial or night time only, without presence of adrenergic triggers) and mixed (combination of vagal and adrenergic triggers). Vagal AF was found in 91 patients (6%), adrenergic in 229 patients (15%) and mixed in 175 (12%) patients. Underlying heart disease was equally prevalent in the three groups. Among patients with vagal AF, 73% were treated with non-recommended drugs according to the guidelines. In vagal AF, non-recommended treatment was associated with a shift to persistent or permanent AF in 19% of the patients, compared with none in the group receiving recommended treatment ($P = 0.06$).

Conclusion This study is the first to address the issue of autonomic trigger patterns and AF in a large population. Autonomic trigger patterns were seen frequently in paroxysmal AF patients. Autonomic influences should be taken into consideration since non-recommended treatment may result in aggravation of vagal AF.

Keywords Atrial fibrillation • Autonomic nervous system • Guideline adherence • Antiarrhythmia agents • Vagal • Adrenergic

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. The condition is frequently associated with structural heart disease, although a substantial number of patients have no underlying heart disease.[1] The autonomic nervous system is known to contribute to the initiation, perpetuation, ventricular response rate, and termination of AF, but its precise role remains controversial.

While the data are mainly empiric, there are two types of autonomic induced AF pointed out in the literature. Coumel and coworkers[2–6] described adrenergic and vagal forms of AF. They reported that the adrenergic mediated episodes of AF are typically triggered by exercise and emotional stress, commonly associated with polyuria, and occur mainly during the day. Adrenergic AF is described to occur in the presence of heart disease.[7] The vagal form is characterized by male predominance, younger age, minimal tendency to progress to permanent AF, and onset at rest or at night and after intake of food or alcohol. Episodes of vagal AF are typically preceded by progressive bradycardia. Studies using heart rate variability have confirmed vagal and adrenergic modes of onset of AF.[8–11] Furthermore, there is support

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for the notion that autonomic modulation influences early recurrences after electrical cardioversion.[12,13]

Epidemiologic data on the prevalence or prognosis of autonomic AF are presently lacking. Furthermore, there is no controlled study examining the response to therapy in vagal or adrenergic AF. However, as in the previous guidelines, the 2006 ACC/AHA/ESC guidelines for the management of patients with AF contain specific recommendations regarding the medical treatment of patients with vagal or adrenergic AF.[14] Beta-blocking drugs, sotalol, digitalis and propafenone are considered unsuitable since they may exacerbate the episodes of vagal induced AF, whereas in adrenergic AF drugs with beta-blocking properties are thought to be beneficial. These recommendations are primarily based on assumptions, since controlled studies on this subject are lacking.

The Euro Heart Survey on AF presents a unique overview of AF management in a large group of patients in several European countries.[15] We identified the clinical characteristics and management of patients with paroxysmal AF associated with autonomic triggers among the patients in the Euro Heart Survey. To our knowledge, this study is the first to address the issue of AF triggers, autonomic trigger patterns, their clinical characteristics, management and outcome in a large population AF patients.

Methods

A detailed description of the methods, data collection, validation, and the first results of the Euro Heart Survey on AF have been presented by Nieuwlaat *et al.*[15]

In 2003 and 2004, 5333 AF patients were enrolled in this survey. These patients were enrolled in 182 hospitals among 35 different member countries of the European Society of Cardiology. Inclusion criteria were: age $>$ 18 years and AF on ECG or Holter recording in the previous 12 months or at the time of inclusion. Enrolment of consecutive patients took place at the outpatient clinic, cardiology ward, emergency department, electrical cardioversion department, electrophysiology laboratory, pacemaker and defibrillator implantation department, and cardiac surgery department.

AF was classified in five categories. The arrhythmia was first detected AF in 978 patients, paroxysmal AF in 1517 patients, persistent AF in 1167 patients, permanent AF in 1541 patients and unknown type of AF in 130 patients. In the present study, only the records from patients with paroxysmal AF were evaluated, leaving a study population of 1517 patients.

In the Euro Heart Survey, data were collected from medical records and medical information systems or entered by the attending physician.

The physicians were asked to report whether the following triggers for AF were present: caffeine intake, alcohol intake, inhalation of toxic gas or electrocution, electrolyte disturbances, acute myocardial infarction, exercise, emotion, postprandial occurrence, and sleep apnoea syndrome. Additionally, circadian rhythms were identified to determine whether the arrhythmia occurred during both day and night, during daytime mainly or started during the night (or was present at wake up).

Using the clinical characteristics of patients with autonomic predominance, we defined an adrenergic, a vagal, and a mixed trigger pattern. The adrenergic trigger pattern was defined as follows: initiated by exercise or emotion and/or present mainly during daytime without reported vagal triggers. We classified patients in the vagal group if AF occurred postprandially and/or was present during the night only without presence of any adrenergic triggers. Patients were classified in the mixed AF group when a combination of at least one adrenergic and one vagal trigger was present.

Patient management was performed consistent with common local practice.

The guidelines contest prescription of a beta-blocker, sotalol, digitalis or propafenone in patients with vagal AF. On the other hand, some drugs are recommended for adrenergic AF (i.e. treatment with a beta-blocker, sotalol, digitalis or amiodarone). In the present study, we evaluated the effect of guideline adherence (recommended treatment) and non-compliance with the guidelines (non-recommended treatment) regarding prescription of medication in autonomic AF.

To evaluate regional differences, we divided the patients into three geographical locations: Western, Central and Mediterranean Europe as defined previously.[15]

Statistical analysis

Data analysis was performed with SPSS statistical software (SPSS, Inc., release 12.0.1). Continuous variables are reported as mean $\pm$ standard deviation and categorical variables as observed number of patients (percentage). Whether there was a difference in characteristics, treatment or outcome between the three groups with vagal, adrenergic, and mixed trigger patterns was tested with ANOVA for continuous and χ^2 for categorical variables and these *P*-values are reported in the tables. Post hoc pairwise analysis was performed using Bonferroni and the corresponding *P*-values were reported in the text. When comparing two groups, differences for continuous variables were tested with an independent *t*-test and differences for categorical variables were tested with χ^2. All tests performed were two-sided. Overall, a *P*-value of <0.05 was considered to be statistically significant.

Results

Atrial fibrillation triggers

One or more triggers were reported in 640 (42%) patients with paroxysmal AF. In 535 (35%) patients no triggers were found and in 342 (23%) patients the physician did not verify the presence of triggers. No differences regarding baseline characteristics, medical history, and previous interventions were found between the latter group and patients in whom the presence of triggers was verified by the physician (data not shown).

Exercise and emotion were the most frequently reported triggers of AF *(Figure 1)*. Patients with triggers were somewhat younger compared with the patients in whom no trigger was found. Patients without triggers had less thyroid disease, more often sick sinus syndrome and an implanted pacemaker. No significant differences concerning other baseline characteristics were found (*Table 1)*.

Autonomic trigger patterns

Autonomic trigger pattern according to our definition could be identified in 495 of the patients with paroxysmal AF (33%): in 91 patients (6%) a vagal trigger pattern was present, 229 patients (15%) had an adrenergic trigger pattern, and 175 patients (12%) a mixed trigger pattern (*Table 2*). No differences regarding underlying heart disease, age or other baseline characteristics were found between patients with vagal, adrenergic, and mixed AF.

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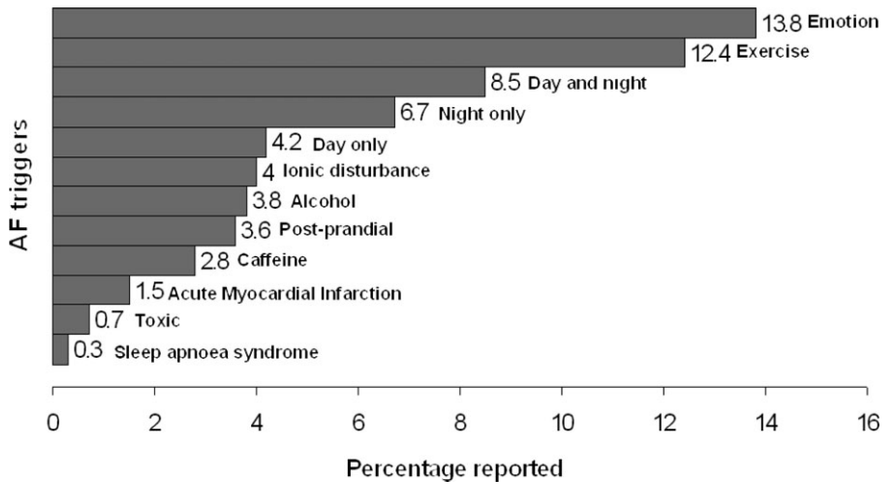

Figure 1 Percentages of triggers reported in patients with paroxysmal atrial fibrillation in the Euro Heart Survey

Table 1 Characteristics of paroxysmal atrial fibrillation (AF) patients with vs. without triggers

	Any trigger	No triggers found	*P*-value
n	640	535	
Age (years)	62 ± 13	64 ± 13	0.012
Female	258 (40%)	238 (45%)	0.149
Lone AF	102 (16%)	86 (16%)	0.870
Underlying heart disease			
Heart failure	156 (25%)	114 (21%)	0.222
Coronary artery disease	210 (33%)	162 (30%)	0.337
Valvular heart disease	118 (19%)	91 (17%)	0.575
Mitral stenosis	41 (6%)	26 (5%)	0.280
Hypertension	414 (65%)	325 (61%)	0.164
Other diseases			
Thyroid disease	36 (6%)	17 (3%)	0.047
Pulmonary disease	82 (13%)	66 (12%)	0.803
Sick sinus syndrome	31 (5%)	43 (8%)	0.023
Peripheral vascular disease	43 (7%)	30 (6%)	0.420
Renal failure	37 (6%)	33 (6%)	0.783
Malignancy	31 (5%)	19 (4%)	0.247
Stroke/TIA[a]	62 (10%)	46 (9%)	0.497
Previous interventions			
Pharmacological cardioversion	328 (51%)	283 (53%)	0.569
Electrical cardioversion	167 (26%)	127 (24%)	0.358
Catheter ablation	37 (6%)	28 (5%)	0.675
Pacemaker	26 (4%)	41 (8%)	0.008

[a]TIA, transient ischaemic attack.

Vagal AF was not restricted to lone AF since hypertension (71%), coronary artery disease (29%) and heart failure (24%) were often present among the patients with a vagal trigger pattern. No differences regarding events during follow-up were found between the three autonomic trigger pattern groups (*Table 3*).

Autonomic trigger patterns and drug therapy

We compared therapy between patients with adrenergic and vagal triggers of AF to investigate the relationship between potential trigger patterns and clinical management. Patients with vagal AF were treated more often with Class Ic anti-arrhythmic drugs compared with patients with adrenergic AF ($P = 0.007$), as suggested by the guidelines. Although not recommended, patients with a vagal trigger pattern were frequently treated with a beta-blocker, sotalol, digoxin or propafenone (*Figure 2*). No differences were found between the prescription of ACE (angiotensin converting enzyme)-inhibitors, AT(angiotensin)II receptor blockers, dihydropyridin calcium channel blockers, diuretics and statins between the vagal and adrenergic AF group. In total, 72% of the patients with vagal AF used non-recommended medication, especially beta-blockers. In the patients with vagal AF, beta-blockers (including sotalol) were prescribed in 51 patients (57%). On the other hand, 36% of the patients with adrenergic AF did not receive a beta-blocker.

In the Euro Heart Survey, physicians were also asked to report 1 year follow-up items regarding worsening of paroxysmal AF to persistent or permanent AF, number of pharmacological cardioversions, number of electrical cardioversions, number of ablations, and the frequency of admissions and consultations. Complete follow-up data were available for 53–70% of the patients with adrenergic AF and 62–73% of the patients having vagal AF depending on each item studied. To evaluate the effect of the choice of medical therapy, we looked at dissimilarities regarding baseline characteristics and outcome at 1-year

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Table 2 Characteristics of patients with an adrenergic, vagal, and mixed trigger pattern

	Adrenergic trigger pattern	Vagal trigger pattern	Mixed trigger pattern	*P*-value
n	229	91	175	
Age (years)	62 ± 13	62 ± 14	62 ± 13	0.609
Female	94 (41%)	38 (42%)	73 (42%)	0.988
Body weight	81 ± 15	80 ± 19	80 ± 16	0.906
BMI	27 ± 5	28 ± 6	27 ± 5	0.484
Heart rate at inclusion (when SR) (BPM)	69 ± 13	66 ± 15	69 ± 17	0.533
Heart rate at inclusion (when AF) (BPM)	110 ± 32	109 ± 40	106 ± 29	0.390
Lone AF	35 (15%)	14 (16%)	37 (21%)	0.268
Underlying heart diseases				
Heart failure	58 (25%)	22 (24%)	34 (20%)	0.368
Coronary artery disease	69 (30%)	26 (29%)	55 (31%)	0.891
Valvular heart disease	43 (19%)	18 (20%)	28 (16%)	0.698
Mitral stenosis	16 (7%)	7 (8%)	8 (5%)	0.508
Hypertension	149 (65%)	65 (71%)	109 (62%)	0.331
Other diseases				
Thyroid disease	12 (6%)	5 (6%)	8 (5%)	0.906
Pulmonary disease	25 (11%)	6 (7%)	22 (13%)	0.322
Sick sinus syndrome	8 (3%)	7 (8%)	10 (6%)	0.261
Peripheral vascular disease	16 (7%)	2 (2%)	12 (7%)	0.220
Renal failure	12 (5%)	5 (6%)	7 (4%)	0.804
Malignancy	7 (3%)	5 (6%)	9 (6%)	0.429
Major bleeding	2 (1%)	1 (1%)	2 (1%)	0.960
Stroke/TIA	25 (11%)	8 (9%)	16 (9%)	0.796
Previous interventions				
Pharmacological cardioversion	125 (55%)	43 (47%)	98 (56%)	0.374
Electrical cardioversion	63 (28%)	22 (24%)	62 (35%)	0.107
Catheter ablation	12 (5%)	3 (3%)	17 (10%)	0.082
Pacemaker	8 (4%)	7 (5%)	0	0.542

BMI, body mass index; SR, sinus rhythm; BPM, beats per minute; TIA, transient ischaemic attack.

Table 3 Events during follow-up of patients with an adrenergic, vagal, and mixed trigger pattern

	Adrenergic trigger pattern	Vagal trigger pattern	Mixed trigger pattern	*P*-value
n	229	91	175	
Outcome at 1 year				
Survival	170 (97%)	74 (96%)	142 (99%)	0.214
Pharmacological cardioversion	31 (22%)	17 (25%)	30 (23%)	0.847
Electrical cardioversion	19 (14%)	9 (13%)	18 (14%)	0.991
Catheter ablation	12 (8%)	8 (12%)	17 (13%)	0.278
Admission for AF	50 (41%)	25 (43%)	55 (51%)	0.358
Cardiovascular hospitalizations	65 (52%)	29 (50%)	65 (60%)	0.444
AF consultations during follow-up	115 (79%)	49 (77%)	106 (88%)	0.093
AF type worsening at 1 year (persistent or permanent)	22 (14%)	9 (14%)	18 (14%)	0.995
Symptoms at 1 year	60 (40%)	20 (31%)	59 (46%)	0.141

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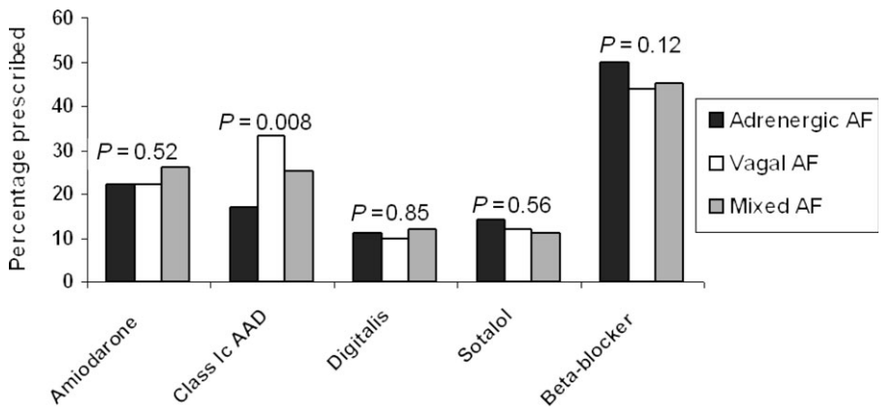

Figure 2 Prescription of medication in autonomic atrial fibrillation (AAD: anti-arrhythmic drugs)

follow-up among patients with autonomic trigger patterns receiving recommended and non-recommended treatment. As represented in *Table 4*, there were no significant differences in patient characteristics and medication in patients with vagal AF receiving recommended and non-recommended therapy. Non-recommended treatment was associated with a clear trend towards aggravation of vagal AF. In the vagally mediated paroxysmal AF patients, non-recommended treatment was associated with a deterioration to persistent or permanent AF in 19% of the patients during 1-year follow-up, compared with none in the group treated with recommended medication ($P = 0.06$) (*Figure 3*).

In the adrenergic group, more heart failure and coronary artery disease were present in the patients receiving recommended therapy. No difference in progression to persistent or permanent AF was found in adrenergic AF between the groups treated with recommended and non-recommended medication. Concerning the other indicators of outcome such as AF interventions, hospitalizations and consultations, no major differences were found between recommended and non-recommended treatment in both vagal and adrenergic AF.

Regional disparity and (non-)recommended treatment

A few differences between European regions were observed. The largest number of patients in whom the physician did not verify the presence of triggers resided in Western Europe (54%) compared with only 21% in Central Europe and 25% in Mediterranean Europe. In case the presence of triggers was verified by the physician, the relative distribution of triggers and autonomic trigger patterns were similar across Europe (data not shown).

In the Mediterranean countries, a larger proportion of the population was treated in accordance with the ACC/AHA/ESC guidelines for the management of patients with vagal AF as 41% of the patients received recommended treatment according to the guidelines compared with 20% in Central Europe and 19% in Western Europe. In adrenergic AF, the percentage of patients receiving recommended medication was similar in Central, Mediterranean, and Western Europe.

Discussion

The Euro Heart Survey provides a unique insight into the characteristics of patients with triggers for AF and the way they are presently treated. To our knowledge, this is the first large observational study to provide an overall picture of autonomic trigger patterns for AF, its management and outcome. Physicians reported triggers in 42% of paroxysmal AF patients in the survey. An autonomic trigger pattern (adrenergic, vagal or mixed) was present in 33% of all patients. In contrast to the general opinion on autonomic AF, there were no differences in patient characteristics and prevalence of concomitant heart disease in patients with vagal or adrenergic AF. In fact, we recorded heart failure, coronary artery disease, valvular heart disease and hypertension in as many patients having the vagal form of the arrhythmia as in patients with adrenergic AF. Also, both patient groups are of similar age. Despite the fact that physicians themselves reported the triggers in their patients, they presumably did not always correctly recognize the autonomic pattern, since 72% of the patients with vagal AF and 20% of the patients with adrenergic AF did not receive the recommended medication according to the ACC/AHA/ESC guidelines for the management of patients with AF.[14] Although patients seem to respond well to what is considered non-recommended treatment, the present data suggest that especially in patients with vagal AF, this may be detrimental because of potential aggravation of the arrhythmia pattern. Among the patients with adrenergic AF, no significant differences in outcome (or trends) were found between the patients using recommended and non-recommended treatment. One could hypothesize that this would reduce the clinical relevance of adrenergic AF. On the other hand, adrenergic AF patients receiving recommended medication had more underlying heart disease such as coronary artery disease or heart failure (*Table 4*) making them more vulnerable for recurrent AF and the development of more sustained forms of the arrhythmia.

Patients with triggers for atrial fibrillation

The presence of paroxysmal AF is an interplay between initiating triggers and a perpetuating substrate. An arrhythmogenic substrate

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Table 4 Characteristics and outcome of paroxysmal AF patients with a vagal or adrenergic trigger pattern who received recommended and non-recommended treatment

	Adrenergic trigger pattern (n = 221)			Vagal trigger pattern (n = 91)		
	Non-recommended treatment group	Recommended treatment group	P-value	Non-recommended treatment group	Recommended treatment group	P-value
n	43	178		66	24	
Age (years) (SD)	59 (15)	62 (12)	0.080	63 (14)	61 (14)	0.465
Female	18 (42%)	73 (41%)	0.919	31 (47%)	7 (30%)	0.130
Underlying heart diseases						
Heart failure	6 (14%)	51 (29%)	0.046	18 (27%)	4 (17%)	0.301
Coronary disease	5 (12%)	64 (36%)	0.002	19 (29%)	7 (29%)	0.972
Valvular disease	7 (16%)	34 (19%)	0.669	14 (21%)	4 (17%)	0.634
Mitral stenosis	4 (9%)	11 (6%)	0.471	5 (8%)	2 (8%)	0.906
Hypertension	24 (56%)	123 (69%)	0.098	49 (74%)	16 (67%)	0.478
Other diseases						
Thyroid disease	1 (2%)	11 (7%)	0.304	5 (8%)	0	0.194
COPD	4 (9%)	20 (11%)	0.706	4 (6%)	2 (9%)	0.664
Medication						
ACE-inhibitor	20 (47%)	94 (53%)	0.458	31 (47%)	13 (54%)	0.546
ATII-receptor blocker	4 (9%)	17 (10%)	0.960	9 (14%)	2 (8%)	0.497
Statins	8 (19%)	48 (27%)	0.258	20 (30%)	5 (21%)	0.375
Diuretics	11 (26%)	67 (38%)	0.138	29 (44%)	9 (38%)	0.584
Anti-arrhythmic drugs						
Amiodarone	0 (0%)	48 (27%)	<0.001	12 (18%)	8 (33%)	0.126
Disopyramide	1 (2%)	0 (0%)	0.041	0	0	–
Quinidine	1 (2%)	1 (1%)	0.273	0	0	–
Flecainide	6 (14%)	10 (6%)	0.058	6 (9%)	6 (25%)	0.05
Propafenone	12 (28%)	10 (6%)	<0.001	18 (27%)	0	0.004
Outcome at 1 year						
Cardioversion	11 (38%)	30 (28%)	0.289	14 (29%)	7 (41%)	0.336
Catheter ablation	3 (10%)	9 (7%)	0.652	5 (10%)	2 (12%)	0.857
Admission for AF	10 (48%)	39 (41%)	0.556	19 (45%)	6 (40%)	0.726
Cardiovascular hospitalizations	12 (52%)	51 (53%)	0.972	22 (52%)	7 (47%)	0.704
AF consultations during follow-up	20 (74%)	90 (79%)	0.582	38 (83%)	11 (65%)	0.129
AF type worsening at 1 year (persistent or permanent)	5 (16%)	16 (14%)	0.765	9 (19%)	0	0.062

COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme; ATII, angiotensin II.

may develop with age or with prolonged exposure to underlying heart disease.[16] Triggers may develop from high adrenergic tone, which may also increase the awareness of palpitations in case of an arrhythmia. In our study, patients in whom triggers were reported were somewhat younger and more often had thyroid disease. In contrast, patients with reported triggers of AF less often had sick sinus syndrome and pacemaker implantation, possibly because of their lower age. In case of pacemaker implantation, symptoms and therefore reported trigger-frequency may decrease.

At the time of the survey, physicians might have been less aware of the relation between obstructive sleep apnoea syndrome (OSAS) and AF, since the reported incidence is low. On the other hand, considering the relatively normal BMI (body mass index) of patients in this European survey, the prevalence of OSAS may have been truly low.

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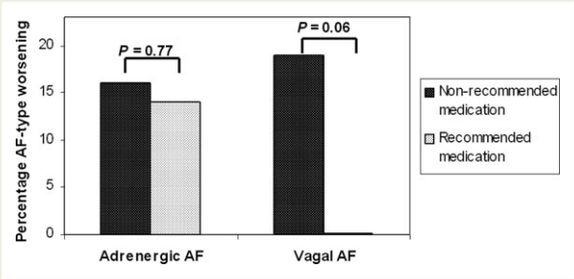

Figure 3 Effect of (non-)recommended treatment on worsening of atrial fibrillation (AF)-type (shift from paroxysmal AF at baseline to persistent or permanent AF at follow-up or from persistent AF at baseline to permanent AF at follow-up)

Clinical characteristics of patients with vagal or adrenergic atrial fibrillation

The precise role of the autonomic nervous system in the initiation, perpetuation, and termination of AF remains undefined.[7–10,17] The clinical history is a consistent tool to determine which type of autonomic predominance results in a destabilization of the arrhythmogenic substrate.[3]

The clinical characteristics of vagal and adrenergic AF have been described previously. According to Coumel *et al.*,[4] the vagally induced form of AF would occur typically in middle aged males without demonstrable heart disease, and arises more frequently than adrenergic AF. Adrenergic AF would typically occur in the presence of heart disease and can be associated with disorders such as pheochromocytoma and hyperthyroidism.[7] Our results reveal a different picture of these patients: vagal AF occurred in elderly men whose age did not differ from that in the general Euro Heart Survey population. In addition, many of the vagal AF patients had underlying heart disease. Furthermore, adrenergic AF was identified more frequently among the patients of the Euro Heart Survey than vagal AF (ratio 3:2).

Drug therapy and autonomic atrial fibrillation

As the initiation of AF can be related to autonomic balance, this balance must be taken into consideration in the choice of medication to treat the arrhythmia.[5]

The guidelines on AF treatment recommend a different approach concerning the choice of rate-control and anti-arrhythmic drugs in patients with vagal or adrenergic AF.[14] The recommendations seem to be based on empirical evidence since controlled studies on the effect of different drugs in autonomic induced AF are lacking. In the vagally mediated form of the arrhythmia, the guidelines advice to avoid treatment with beta-blocking drugs, sotalol, propafenone or digitalis, as they may worsen symptoms. Among the patients with adrenergic AF, the guidelines advise beta-blockers as first line treatment, followed by sotalol or amiodarone.

The results from the present study suggest that physicians do not seem to choose drug therapy based upon the autonomic pattern of induction of AF. Most remarkable was the finding that the frequency of beta-blocker administration was not altered by the presence of vagal triggers for AF (44% still received beta-blocker) or sympathetic triggers (36% did not receive a beta-blocker).

In general, physicians want to prevent high heart rates during recurrences of AF. Also, during treatment with Class Ic anti-arrhythmic drugs, rate-control medication is advised to prevent 1:1 conduction in the case of Ic atrial flutter. Therefore, rate-controlling drugs such as beta-blockers and digitalis are used frequently. However, non-dihydropiridine calcium channel blockers (i.e. verapamil and diltiazem) could be used as safe alternatives. Furthermore, the need for rate control in patients with paroxysmal vagal AF may be less, since the heart rate during vagal AF is usually not as high as in adrenergic AF.[18] On the other hand, vagal AF patients also suffer frequently from underlying heart disease necessitating the application of a beta-blocker.

Among the patients with adrenergic AF, use of recommended treatment was particularly seen in patients suffering from chronic heart failure and coronary artery disease. We assume that this is explained by the fact that a beta-blocker is indicated in both heart failure and coronary disease.

Although only borderline significant, there is a clear trend towards deterioration of the arrhythmia to persistent or even permanent AF in patients with vagal AF receiving non-recommended treatment. Clinical consumption (electrical or pharmacological cardioversions, catheter ablations, hospitalizations, consultations) was equal in both groups receiving recommended and non-recommended medication.

Study limitations

In this non-randomized study, we performed a subgroup analysis of the Euro Heart Survey. As a result, our findings should be interpreted with care. An observed poor statistical significance in a subgroup may be a result of lack of power due to small numbers rather than absence of a relation. On the other hand, experiment-wise type I error may be the result of multiple testing in this study.

Regrettably, there are no quantitative measures known to reproduce vagal or adrenergic predominance. The assessment of triggers in patients with AF is challenging. Adequate history taking is essential in the identification of trigger patterns as it might be difficult to discriminate between triggers that initiate the arrhythmia and factors that worsen the symptoms. In clinical practice, triggers such as exercise and emotion can be misinterpreted and wrongly recognized as triggers for AF. The physician has a crucial role in identifying this bias. Our report is based on this clinical judgement by the physician. Since data on triggers were not verified in 23% of the patients, the reported numbers on prevalence of triggers and autonomic trigger patterns are probably underestimated.

Conclusion

The Euro Heart Survey is the first large observational study to provide a description of the clinical characteristics of paroxysmal AF patients having triggers and autonomic trigger patterns, its management, and outcome. An autonomic trigger pattern (vagal or adrenergic) was found in almost one-third of the patients. Patients with vagal AF have similar characteristics to patients with

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adrenergic AF and much more frequently underlying heart disease than previously thought. Physicians do not seem to choose rhythm or rate control medication based upon autonomic trigger pattern of AF. However, the role of autonomic influences should be taken into consideration in order to achieve an optimal management of the disease as non-recommended treatment may result in aggravation of the arrhythmia.

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