Current practice of antiarrhythmic drug therapy for prevention of atrial fibrillation in Europe: The European Heart Rhythm Association survey

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The aim of this survey was to provide insight into current practice regarding the use of antiarrhythmic drugs for atrial fibrillation (AF) among members of the European Heart Rhythm Association research network. Thirty-seven centres responded. Rhythm control was preferred in patients with significant AF-related symptoms by 73% of centres, in all patients after a first detected episode by 59%, and in young patients even if AF was well tolerated by 49% of centres. The most common strategy after successful conversion of the first AF episode was a 'wait-and-see' approach without initiation of antiarrhythmic drugs (49%). Conventional β-blockers were always or sometimes used as first-choice drugs for AF prevention by 76% of centres. Only 11% used dronedarone regularly as a first-choice drug. The diagnostic work-up for exclusion of heart disease prior to initiation of class IC antiarrhythmic drugs was limited. Markers monitored for proarrhythmia risk were QRS duration for class IC drugs (68%) and the QT interval for sotalol and amiodarone (65%). In conclusion, rhythm control is more widely employed than expected. Beta-blockers are widely used for AF prevention in contrast to the limited use of the new drug dronedarone.

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia and represents a major health burden for the society. There is lack of evidence for a superiority of a rhythm control approach aiming at maintenance of sinus rhythm over simple rate control in randomized trials,[1] but appropriate rate vs. rhythm management of AF in the 'real-world' clinical practice is still controversial.[2] Rhythm control is frequently employed in several clinical settings and some possible benefit of this strategy over rate control may be evident.[3,4]

There are several classes of antiarrhythmic drugs, which may be used for prevention of AF and their use in clinical practice shows significant variation. The aim of this survey was to provide insights into current European clinical practice regarding the use of antiarrhythmic drugs for AF.

Results

Thirty-seven centres, which are members of the EHRA EP research network, responded to the survey. There was a wide geographic distribution of the responding centres from 17 countries (six centres from Spain, five from Italy, four each from Denmark and the United Kingdom, three from Belgium, two each from Greece, the Netherlands, and Romania, and one centre from eight other countries or unspecified). Approximately two-thirds (68%) of the responding centres were university hospitals.

Clinical settings, in which rhythm control was used, is shown in *Figure 1*. In patients with a first detected AF episode who had successful cardioversion, 49% of centres followed an initial 'wait-and-see' approach and initiated antiarrhythmic therapy only after one or more recurrences, 14% would wait and recommend 'pill-in-the-pocket' therapy in the case of recurrence, 14% would

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offer short-term prophylactic antiarrhythmic therapy, and 19% would give long-term prophylactic therapy if the patient was considered to be at high risk of recurrent AF. Only 5% of the centres would give long-term prophylactic therapy directly after a first AF episode.

After the failure of the first rhythm control drug, most centres would insist on rhythm control with the majority (65%) trying another rhythm control drug or referring the patient for AF ablation (35%). Only 5% would switch to rate control.

Preferred first-line drugs for prevention of AF in different patient groups are shown in *Figure 2*. A pill-in-the-pocket approach with class IC drugs would be used for AF cardioversion by 76% centres. Before recommending this approach, the majority of centres would first test its efficacy and safety within the hospital setting either routinely (62%) or only in patients with structural heart disease (14%). Only 8% would recommend it without previous testing. The most widely applied regimen for this purpose was oral flecainide (43%) with a initial dose of 100−200 mg followed by an additional dose of 100 mg after 1−2 h if the first one was not

successful or oral propafenone (35%) with an initial dose of 300 mg and an additional dose of 150−300 mg after 1−2 h.

Class IC antiarrhythmic drugs were used with caution in patients with structural heart disease. In patients with coronary artery disease, 51% centres would always avoid them while 35% would avoid them in patients with reduced left ventricular ejection fraction (e.g. <40%). Class IC antiarrhythmic drugs were avoided by the majority of centres (73%) in patients with dilated cardiomyopathy even if left ventricular systolic function was only mildly impaired. The diagnostic work-up in order to confirm the absence of structural heart disease prior to initiation of therapy with class IC antiarrhythmic drugs was limited (*Figure 3*).

Hospitalization was not routinely required for initiation of therapy with class IC antiarrhythmic drugs: 41% of the centres would sometimes initiate therapy with class IC drugs in-hospital, whereas 38% would always initiate therapy on an out-patient basis. Initiation of sotalol therapy occurred in a relatively similar way: 38% of centres would sometimes initiate sotalol therapy in-hospital, whereas 30% would always initiate therapy on an outpatient basis. The remaining centres (32%) initiated sotalol therapy during hospitalization with duration of telemetric monitoring varying from <24 h to >48 h.

Considerable risk of proarrhythmias with antiarrhythmic drug therapy was recognized for class IC antiarrhythmic drugs by 62% centres and for sotalol by 57% centres, whereas only a minority (16%) regarded amiodarone to be associated with a considerable proarrhythmic risk. Main markers monitored for the risk of proarrhythmia were the QRS duration for class IC antiarrhythmic drugs (68%) and the QT interval for sotalol and amiodarone (65%). Prolongation of the QTc interval >500 ms would be the reason for discontinuation of amiodarone therapy at 49% centres, and only excessive QTc interval prolongation >550 ms at 30% centres. Interestingly, 22% did not use the QTc interval as a guide for discontinuation of amiodarone therapy.

Dronedarone was only rarely used for rhythm control: 49% of centres would use it in patients with paroxysmal or persistent AF after failure of other antiarrhythmic drugs, whereas 41% would never use it. Only 11% would use it regularly as one of the first-choice drugs in patients with paroxysmal or persistent
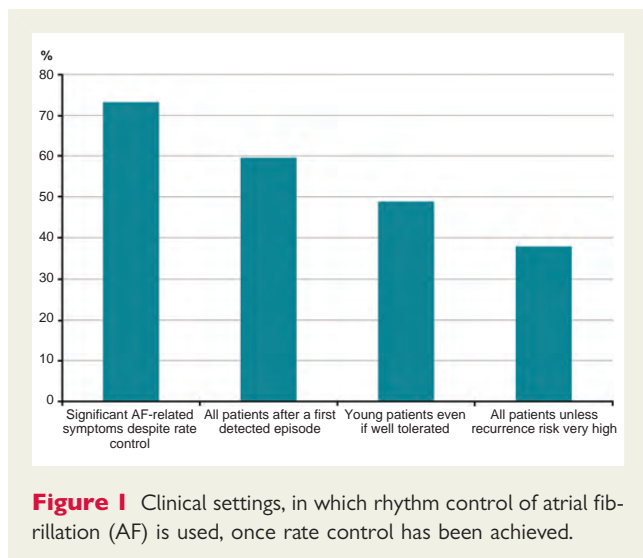
Figure 1 Clinical settings, in which rhythm control of atrial fibrillation (AF) is used, once rate control has been achieved.
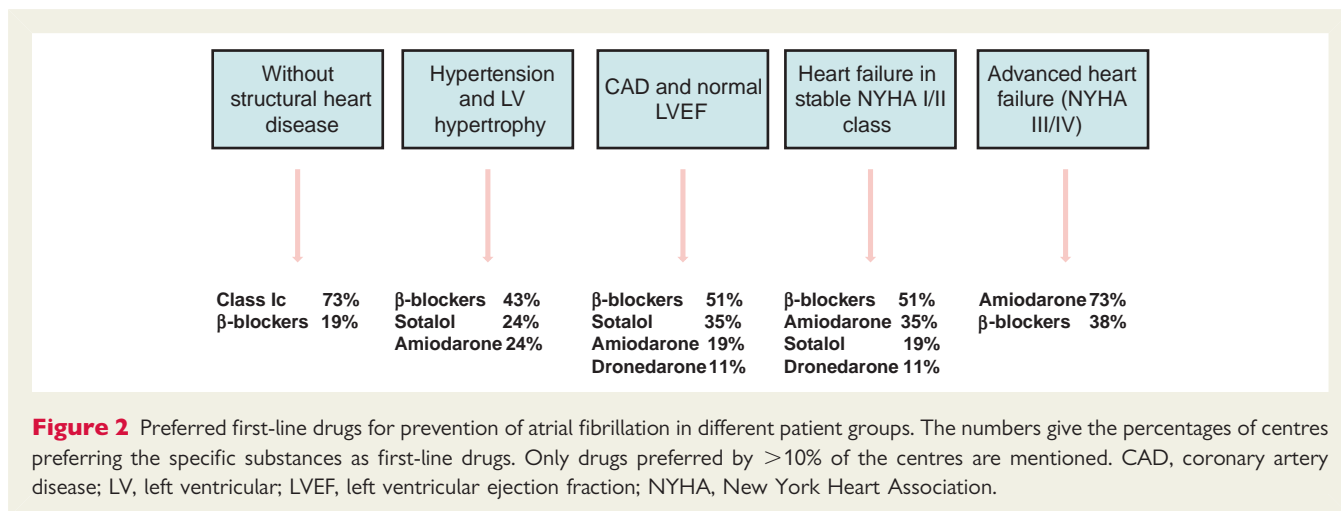
Figure 2 Preferred first-line drugs for prevention of atrial fibrillation in different patient groups. The numbers give the percentages of centres preferring the specific substances as first-line drugs. Only drugs preferred by >10% of the centres are mentioned. CAD, coronary artery disease; LV, left ventricular; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.
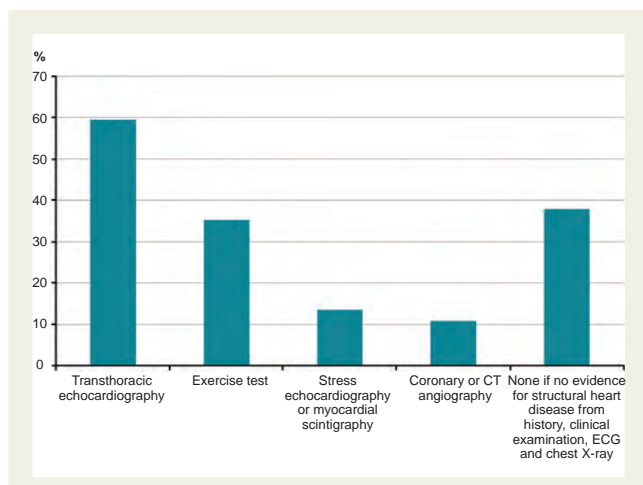
Figure 3 Diagnostic work-up prior to initiation of therapy with class Ic antiarrhythmic drugs in order to confirm the absence of structural heart disease. The figure shows the percentages of centres, which consider the specific examinations to be necessary. CT, computed tomographic; ECG, electrocardiogram.

AF without or with mild-to-moderate heart disease (e.g. hypertension with left ventricular hypertrophy, coronary artery disease with preserved left ventricular ejection fraction).

Conventional β-blockers were widely used as prophylactic antiarrhythmic therapy for AF. Due to low risk associated with this therapy, 76% centres would use β-blockers as first-choice drugs, either always (30%) or sometimes (46%). Only 24% centres would never use them as first-choice drugs due to their low efficacy.

Discussion

A major finding in this survey is the frequent use of rhythm control by the majority of centres, especially in young patients and in patients with a first detected AF episode. Obviously, physicians feel that most patients deserve at least one attempt to achieve sinus rhythm. Approximately one-third of the responding centres even prefer a rhythm control strategy in all patients unless there is a high anticipated risk of recurrence. Thus, this is a wider use of rhythm control than one would expect based on the results of the randomized trials which did not show any survival benefit of this strategy over rate control and the current recommendations for management of patients with AF.[1,5] However, recent studies have shown a potential advantage of rhythm control over rate control, such as a survival benefit in the long-term,[3] a reduced progression rate to persistent or permanent AF,[4] and a lower incidence of stroke or transient ischaemic attack.[6] Yet, the reduction in AF-related symptoms is the main goal with rhythm control therapy, which can be expected if sinus rhythm is maintained. These data are also in agreement with previous findings suggesting the benefit of rhythm control especially in younger patients.[7] It is also interesting that, after choosing rhythm control as the initial strategy, most centres continue this strategy despite the failure of the first attempt and do not switch immediately to rate control.

Despite a relatively wide use of rhythm control in patients with the first detected episode, there is a reluctance to initiate long-term antiarrhythmic drug therapy for AF prevention in these patients after successful conversion to sinus rhythm. Many centres employ a 'wait-and-see approach' instead probably in order to minimize the possible adverse effects.

Regarding the choice of specific antiarrhythmic drugs, the most striking finding is the wide use of conventional β-blockers due to the low associated risk and despite the modest efficacy.[8] Thus, 76% centres always or sometimes use β-blockers as prophylactic therapy for AF. Another interesting finding regarding the choice of specific antiarrhythmic agents is the limited use of dronedarone. Although the drug is recommended by recent guidelines for several patient groups,[9] only 11% use it regularly as one of the first-choice drugs in patients with paroxysmal or persistent AF without or with mild-to-moderate heart disease.

Expectedly, class IC antiarrhythmic drugs are used with great caution in patients with structural heart disease. However, the diagnostic work-up for exclusion of heart disease prior to initiation of therapy with these agents is limited. A significant proportion of centres (38%) consider a basic work-up including patient history, clinical examination, an electrocardiogram (ECG), and chest X-ray sufficient. If further tests are performed, these are mainly transthoracic echocardiography (59% centres) and exercise test for detection of myocardial ischaemia (35% centres).

Hospitalization is not routinely required for initiation of antiarrhythmic drug therapy either with class IC antiarrhythmic agents or sotalol. A significant percentage of centres routinely initiate therapy on an out-patient basis or sometimes during hospitalization. This is somewhat unexpected given the limited diagnostic work-up. Although the majority of centres follow the recommendations[5] and monitor markers of proarrhythmia such as QRS duration for class IC antiarrhythmic drugs (68%) and the QT interval for class III antiarrhythmic drugs (65%), these percentages are lower than expected.

Conclusions

Rhythm control is preferred by many European centres, especially in young patients and in patients with first detected AF episode. After successful conversion of a first AF episode, most centres do not initiate antiarrhythmic therapy. Conventional β-blockers are widely used for AF prevention in contrast to the limited use of dronedarone. The diagnostic work-up for exclusion of heart disease prior to initiation of therapy with class IC antiarrhythmic drugs is surprisingly limited and monitoring of ECG markers for risk of proarrhythmia is not uniformly performed.

Acknowledgements

A list of the Research Network centres can be found on the EHRA website.

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