European Society of Cardiology 2010 Clinical Practice Guidelines on Atrial Fibrillation

An Update on Classification and Pharmacotherapy

Abstract

The European Society of Cardiology guidelines published in 2010 offer an update on the previously published 2006 atrial fibrillation guidelines. The revisions are intended to optimize the understanding of the mechanisms of atrial fibrillation, and consequently the diagnosis and management of this common sustained cardiac arrhythmia, which afflicts up to 1-2% of the general population.

Ongoing research into the pathophysiology of atrial fibrillation and innovations in pharmacotherapy have forced a revised set of non-mandatory but advisory recommendations to guide clinicians and cardiologists along the challenging labyrinth which is atrial fibrillation management and diagnosis. The purpose of this synopsis is to highlight some of the most relevant changes included in the 2010 guidelines in so far as classification and pharmacotherapy of atrial fibrillation is concerned.

Atrial fibrillation, arrhythmia, heart failure, heart disease

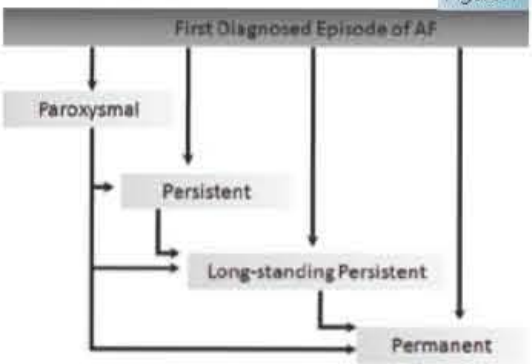
Introduction

The European Society of Cardiology (ESC) guidelines published in 2010 offer an update on the previously published 2006 atrial fibrillation (AF) guidelines. The revisions are intended to optimize the understanding of the mechanisms of AF, and consequently the diagnosis and management of this common sustained cardiac arrhythmia, which afflicts up to 1-2% of the general population.1

Mechanisms of Atrial Fibrillation

The structural remodeling that occurs in the ventricles and atria is the end result of many forms of structural heart disease. Within the atria this translates into proliferation and differentiation of fibroblasts into myofibroblasts and accumulation of surplus connective tissue with eventual fibrosis. These changes produce an electroanatomical substrate which is pervious to multiple small re-entrant circuits and which therefore permits the propagation of AF. Following the onset of AF, the atrial effective refractory period has been shown to shorten within the first days of its onset in addition to a disruption of the normal atrial contractile function.

Figure 1



AF clinical types

The diagram illustrates how a first diagnosed episode of AF may turn out to be any of the 4 clinical sub- types and how the AF categories are not mutually exclusive with patients having paroxysmal AF sometimes moving on to having persistent AF, so on and so forth.

AF=atrial fibrillation. Adapted from Camm AJ et al.1

Clinical Types of AF

The 2010 ESC guidelines offer a modified nomenclature for classification of the AF clinical types (Figure

1). In particular the guidelines distinguish between:

1) Fist diagnosed AF: which represents the first ever episode of AF at the time of initial presentation irrespective of its duration or symptom severity.
2) Paroxysmal AF: representing AF which self-terminates within a maximum of 7 days (although in most cases self-termination occurs within the first 48 hours).
3) Persistent AF: representing non-self-terminating AF which either lasts longer than 7 days, or which requires pharmacological or electrical cardioversion before this time.
4) Long-standing Persistent AF: refers to persistent AF which has been present for ≥1 year before the implementation of a rhythm control strategy is contemplated.
5) Permanent AF: refers to established, accepted AF where both the patient and physician have opted not to pursue any rhythm control strategies.

Type and Severity of Symptoms

The 2010 guidelines place special emphasis on the presence and severity of AF-related symptoms and recommend tailoring the management of AF in such a way as to achieve maximum possible symptom relief. The European Heart Rhythm Association Score of AF-related symptoms2 (Table 1) provides an unambiguous description of AF-related symptom severity.

Antithrombotic Management of AF

The CHADS2 score (cardiac failure, hypertension, age, diabetes, stroke) risk index3 is recommended in these guidelines as a rapid and initial risk assessment tool for cerebrovascular events and transient ischaemic attacks in patients with non-valvular AF. Any patient having a score ≥2 will benefit from the use of chronic oral anticoagulant therapy (OAC) with a vitamin K antagonist (VKA), aiming to maintain a target international normalized ratio (INR) of 2.5, and a range of 2.0-3.0. The greatest limitation of the CHADS2 score lies in its propensity for classifying a disproportionate number of patients within the 'grey-zone' of moderate risk for cerebrovascular events at a score of 1, thereby plunging many a physician into the much dreaded VKA-versus-aspirin conundrum.

The CHA2DS2-VASc score4 (Table 2) employs a more 'risk

Table 1

EHRA Class	Definition
EHRA Class I	No symptoms
EHRA Class II	Mild symptoms; Normal daily activity not affected
EHRA Class III	Severe symptoms; Normal daily activity affected
EHRA Class IV	Disabling symptoms; Normal daily activity discontinued

EHRA score of AF-related symptoms. Adapted from Kirchhof P et al.2

factor-based' approach to the categorization of patients with non-valvular AF and this scheme is the one most prominently campaigned for by the ESC.
In patients with non-valvular AF, a CHA2DS2-VASc score of ≥2 would argue in favour of OAC therapy. One major risk factor would alone confer such a score, as would alternatively two cumulative clinically relevant but non-major risk factors. In either scenario, use of chronic OAC for thrombophylaxis would be justified.
In summary, the guidelines recommend that with a CHADS2 score ≥2, chronic OAC therapy should be initiated, but in patients scoring a CHADS2 of 0-1, a second more comprehensive risk scoring tool should be employed (CHA2DS2-VASc) to determine whether a subject benefits most from OAC as opposed to Aspirin or no antithrombotic therapy (Figure 2).

The HAS-BLED score5 (Table 3) is recommended as a simple bleeding risk score for AF patients, whereby a score ≥3 indicates high risk and calls for caution with the use of oral VKAs.

Long-term Control of Rate and Rhythm in AF

The 2010 guidelines underscore that ventricular rate control in AF is cardinal in all cases unless the heart rate during AF is naturally slow. Additionally rhythm control may be added on to rate control where the patient remains symptomatic despite adequate rate control; alternatively it may be deemed appropriate to choose rhythm control over rate control as the optimal management strategy based on factors such as younger age, symptomatology and higher activity levels. Broadly speaking, those younger patients with symptomatic paroxysmal AF in the absence of significant structural heart disease are usually earmarked for rhythm control. Conversely, patients with accepted permanent AF are usually scheduled to receive rate control with their designation changing to 'long- standing' persistent AF if a later trial of rhythm control is attempted.
A large body of evidence now exists6-12 to dispel the archaic myth which made rhythm control the unchallenged prime end-point in AF management and which relegated rate control strategies to a lackluster division. This newly-found egalitarianism is fuelled by a new appreciation of the importance of patient-tailored therapy taking into consideration factors such as patient preference, level of physical activity and quality of life scores.

Recommended Drugs for Long-term Rate Control

• Bvetablockers
Particularly in patients with high adrenergic tone or angina in association with AF.
Recommended agents include: Metoprolol, Bisoprolol, Atenolol, Propanolol and Carvedilol.

• Non-dihydropyridine calcium channel blockers
Effective for acute and chronic rate control of AF. These drugs are to be avoided in patients with systolic heart failure in view of their negatively inotropic effect.
Recommended agents include: Verapamil and Diltiazem.
•Digoxin
Effective for heart rate control at rest but not during exercise. The potentially life-threatening adverse effects and propensity for drug interactions ascribed to digoxin dictates a cautious introduction in properly selected patient groups.

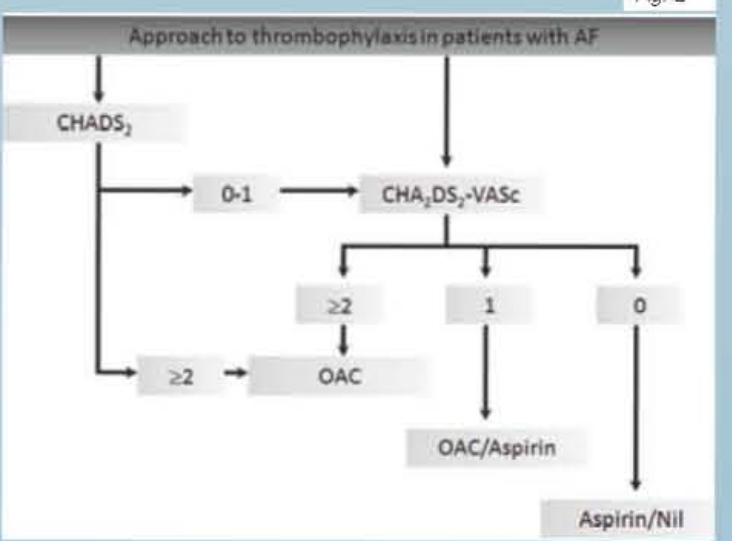
•Dronaderone
Perhaps one of the most noteworthy advances of the 2010 ESC guidelines is the inclusion of the recently approved dronaderone as an alternative rate controlling drug for

Table 2

Risk Factor	Attributable Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age >75	2
Diabetes Mellitus	1
Stroke/TIA/systemic thrombo-embolism	2
Vascular disease	1
Age 65-74	1
Sex **C**ategory (female sex)	1
Maximum score	9

CHA2DS2-VASc Scoring System.
Maximum possible score using the CHA2DS2-VASc Scoring System is 9.
Major risk factors are displayed inside dark grey cells.
Clinically relevant non-major risk factors are displayed inside light grey cells.
Congestive heart failure is arbitrarily defined as left ventricular (LV) ejection fraction (EF) ≤40%.
Vascular disease encompasses any of: myocardial infarction, complex aortic plaque and peripheral artery disease.
LV=left ventricular; TIA=transient ischaemic attack.

Fig. 2



With a CHA2DS2-VASc score of 1, the recommendations are in favour of either OAC or aspirin 75-325mg daily. With a CHA2DS2-VASc score of 0, the recommendations are in favour of either aspirin 75-325mg daily or no antithrombotic therapy. Adapted from Camm AJ et al.1
AF=atrial fibrillation; OAC=oral anticoagulation;

Table 3

Letter	Clinical Characteristic	Points Attributed
H	Hypertension	1
A	Abnormal Renal Function and/or	1
	Abnormal Liver Function	1
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (age >65 years)	1
D	Drugs and/or	1
	Alcohol	1
	Maximum score	9

HAS-BLED score adapted from Pisters et al.5

chronic management of AF. It effectively controls ventricular rate both at rest and during exercise with these effects being additive to those of other rate controlling drugs (Dronaderone is not currently approved for rate control in permanent AF)
Dronaderone is a multichannel blocker active at the sodium, potassium and calcium channels which is also endowed with non-competitive antiadrenergic activity.

•Amiodarone
Effective as a rate controlling agent being particularly suited for intravenous administration in the haemodynamically-ill AF sufferer. It should be considered for long term ventricular rate control only if all other measures have failed and in this context the burden of its innumerable extracardiac adverse events must be borne in mind.

Recommended Drugs for Long-term Rhythm Control
The new 2010 guidelines essentially eliminate quinidine from the rhythm controlling armamentarium of drugs and instead propose dronaderone as one of the emerging therapeutic options for achieving and maintaining sinus rhythm.

•Beta-blockers other than Sotalol
Only modestly effective in preventing recurrent AF except in the setting of thyrotoxicosis and exercise- induced, adrenergic, lone AF where they have a specific and valid role. Their use is limited by contraindications in the presence of significant left ventricular hypertrophy, systolic heart failure and pre-existing QT prolongation.

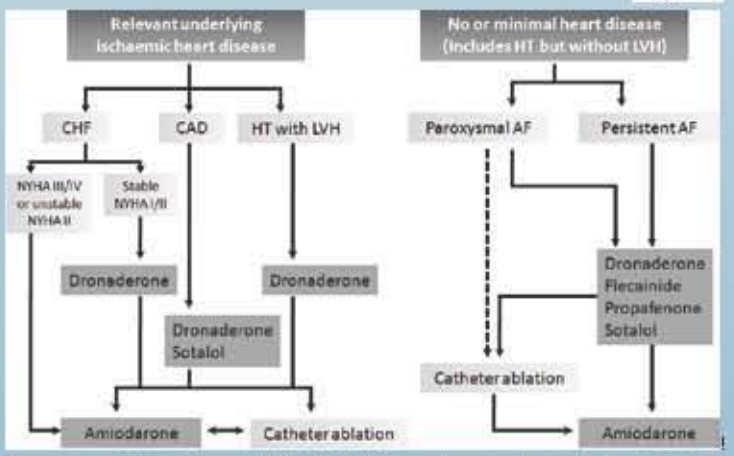
•Flecainide
Safe in the absence of structural heart disease and contraindicated for use in hearts with impaired systolic function and coronary artery disease.

•Propafenone
As for flecainide, propafenone is considered safe in the absence of structural heart disease and contraindicated for use in hearts with impaired systolic function and coronary artery disease.

•Amiodarone
Amiodarone is superior to propafenone and sotalol at preventing recurrent AF and is particularly indicated in symptomatic sufferers where other antiarrhythmic agents have failed to maintain sinus rhythm. It is one of only a few antiarrhythmics which is not contraindicated in the presence of structural heart disease and heart failure. The attendant adverse drug reactions of amiodarone therapy together with its potential interactions with oral VKAs and digoxin beckon watchful vigilance of all patients and their doctors.

•Sotalol
Sotalol has a role in preventing recurrent AF but it's proarrhythmic adverse effects become especially taxing in patients with electrolyte abnormalities, particularly hypokalaemia and hypomagnesaemia. Unlike amiodarone it's use is considered imprudent in patients with structural heart disease and systolic heart failure.

Fig. 3



Summary of recommendation for choice of antiarrhythmic drug therapy in AF patients with and without structural heart disease. Adapted from Camm AJ et al.1
HT=hypertension; AF=atrial fibrillation; CHF=congestive heart failure; CAD=coronary artery disease; LVH=left ventricular hypertrophy; NYHA=New York Heart Association.

•Dronaderone
Admittedly less effective at maintaining sinus rhythm than amiodarone13,14 but far less toxic to the thyroid gland, central nervous system, skin and eyes, which equates to better tolerability and a smaller incidence of premature drug discontinuation. It is contraindicated in patients with New York Heart Association (NYHA) class III15 or more and in unstable heart failure patients but is considered safe in patients with acute coronary syndromes, chronic stable angina, hypertensive heart disease and stable NYHA class I-II heart failure (Figure 3).

Conclusion
Ongoing research into the pathophysiology of AF and innovations in pharmacotherapy have forced a revised set of non-mandatory but advisory recommendations to guide clinicians and cardiologists along the complex labyrinth which is AF management and diagnosis. The purpose of this synopsis was to highlight some of the most relevant changes included in the ESC 2010 guidelines in so far as classification and pharmacotherapy of AF is concerned, while encouraging a more insightful review of the full-text guidance offered by the ESC Committee for Practice Guidelines. For the complete guidelines visit www.escardio.org.

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