OVERVIEW

What is New in the ESC Guidelines for the Management of Atrial Fibrillation

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The European Society of Cardiology (ESC) and the European Heart Rhythm Association (EHRA) have developed the 2010 Clinical Practice Guidelines covering atrial fibrillation (AF),[1] the most common cardiac arrhythmia occurring in 1-2% of the general population. Advance has been made regarding the dynamic development of AF from a preclinical state to an irreversible cardiac arrhythmia and a novel classification of AF has been adopted based on the presentation and duration of the arrhythmia: *first diagnosed*, *paroxysmal*, *persistent*, *long-standing persistent* and *permanent* AF are the 5 types of AF in use for clinical management of patients with AF.

Structural and electrical remodelling are hallmarks of the pathophysiological changes facilitating the initiation and perpetuation of AF. While atrial fibrosis was the main cause of nonhomogeneity of conduction according to earlier ESC guidelines, nowadays any kind of structural abnormality (inflammatory changes, amyloid deposit, apoptosis, necrosis, hypertrophy, microvascular changes, etc.) is believed to trigger the electrical dissociation between muscle bundles and permit small re-entrant circuits to stabilize the arrhythmia.[2] The adage 'atrial fibrillation begets atrial fibrillation' describes electrical remodelling due to shortening of atrial refractory period, which is attributed to down-regulation of the L-type Ca^{2+} inward current and up-regulation of inward rectifier K^{+} currents. Although the exact role of the genome in the pathogenesis of AF is not known, numerous inherited cardiac syndromes and mutations have lately been associated with AF and should be elucidated. Mutations in the gene coding for atrial natriuretic peptide, loss of function mutations in the cardiac sodium channel gene SCN5A or gain of function mutations in the cardiac potassium channel are related to familial AF and genetic loci close to the PITX2 and ZFHX3 genes are currently associated with enhanced risk for cardioembolic stroke.

A new simple clinical tool for the diagnostic evaluation of patients with the 'arrhythmia absoluta' has been introduced in the present guidelines, the EHRA score,[3] which drives the decision for acute restoration of sinus rhythm or acute management of ventricular rate depending on the severity of symptoms. Patients with different types of AF are regarded to have a risk for stroke and thromboembolism according to their 'major' (previously referred to as 'high': previous stroke/TIA or systemic embolism, age≥75 years) and 'clinically relevant non-major' (previously referred to as 'moderate': heart failure or severe LV systolic dysfunction, hypertension, diabetes mellitus, age 65-74 years, female sex, vascular disease) risk factors no matter whether they suffer from paroxysmal, persistent or permanent AF. The 2006 guidelines for the management of AF introduced the $CHADS_2$ score and the 2010 guidelines recommend its use particularly to primary care physicians and non-specialists, because it is a simple and easily remembered score of assessing stroke risk and beginning oral anticoagulant therapy (OAC) when $CHADS_2$ score ≥2 (Table 1). In patients with a $CHADS_2$ score of 0-1 it is recommended to use the CHA_2DS_2-VASC score[4] which provides a more detailed stroke risk assessment, taking into account congestive heart failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65-74 and sex category (female). Patients with CHA_2DS_2-VASC score 1 should take either OAC or aspirin 75-325 mg/day, while those with score 0 should rather take no antithrombotic therapy (Table 2). An assessment of bleeding is essential at the initiation and follow-up of antithrombotic therapy; the HAS-BLED score (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly >65 years, drugs or alcohol consumption) derived from the EuroHeart Survey,[5] is a simple score recommended in current guidelines for anticoagulated patients (score ≥3 indicates caution and regular review of INR) (Table 3). Patients with AF and primary percutaneous coronary intervention (PCI) due to acute ST (or non-ST) segment elevation myocardial infarction should take triple therapy (VKA, aspirin and clopidogrel) in the initial period (3-6 months) or for longer in selected patients at low bleeding risk, followed by longer therapy (up to 12 months) with VKA plus clopidogrel 75 mg/day (or alternatively aspirin 75-100 mg/day). In patients with AF and elective PCI with bare-metal stents, triple therapy (VKA, aspirin and clopidogrel) is recommended for 4 weeks, followed by long-term therapy (12 months) with VKA plus clopidogrel 75 mg/day (or alternatively aspirin 75-100 mg/day).When drug-eluting stents are used, triple therapy should be administered for ≥3 months for an '-olimus' (sirolimus, everolimus, tacrolimus) type eluting stent and at least 6 months for a paclitaxel eluting stent.[6] In the RELY study dabigatran 110 mg twice daily was non-inferior to VKA for the prevention of stroke/systemic embolism and had lower rates of major hemorrhage compared with VKA.

$CHADS_2$ score

•Cardiac failure → 1
•Hypertension → 1
•Age → 1
•Diabetes → 1
•Stroke or TIA → 2

Score 0 : low risk
Score 1 : moderate risk
Score ≥2 : high risk

Table 1. $CHADS_2$ score parameters

CHA_2DS_2VASC score

- Score ≥2: OAC
- Score 1: OAC or aspirin (preferably OAC)
- Score 0: no therapy or aspirin

Risk factor	*Score*
Congestive heart failure or LV dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thromboembolism	2
Vascular disease	1
Age 65-74	1
Sex (female)	1

Table 2. CHA_2DS_2-VASC score definition

HAS-BLED score

Hypertension → 1
Abnormal renal or liver function → 1 or 2
Stroke → 1
Bleeding → 1
Labile INR → 1
Elderly (>65) → 1
Drugs, alcohol → 1or 2

High risk patients (score ≥3) should receive antithrombotic therapy with caution

Table 3. HAS-BLED score definition

Apart from adequate antithrombotic therapy, at the beginning of patients' management, a decision should be made upon the restoration and maintenance of sinus rhythm. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)[7], the RAte Control versus Electrical cardioversion for persistent atrial fibrillation (RACE)[8], the Pharmacologic Intervention in Atrial Fibrillation (PIAF)[9] and the Strategies of Treatment of Atrial Fibrillation (STAF)[10] trials found no differences in quality of life between rhythm and rate control. Although expected at the outset of trials, development of heart failure and mortality were not different between rate and rhythm control in the AFFIRM, RACE or Atrial Fibrillation and Congestive Heart Failure (AF-CHF)[11] trials; post-hoc analysis suggests that deleterious effects of antiarrhythmic drugs and progression of underlying cardiac disease explain these findings. Furthermore, previous guidelines recommended strict rate control (60-80 bpm at rest, 90-115 bpm during exercise) but the RACE II[12] trial did not identify a benefit of strict over lenient (initially aiming at resting heart rate <110 bpm and further reduction of ventricular rate until symptoms become tolerable) rate control. Apart from β-blockers and non-dihydropyridine calcium channel blockers that are useful in both acute and long-term rate control, amiodarone is an effective rate control drug (usually initiated for rhythm control, it may be continued for patients who have lapsed into permanent AF only when safer agents are unsuitable)[1] and a new drug, dronedarone, may also effectively reduce heart rate at rest, during exercise and during AF relapses. The choice of rhythm control therapy depends on underlying heart disease and includes dronedarone, which inhibits sodium – potassium – calcium channels and was proven to be less effective in the maintenance of sinus rhythm but also less toxic than amiodarone in the DIONYSOS trial.[13] Current guidelines recommend dronedarone as the first antiarrhythmic option for patients with symptomatic AF and underlying cardiovascular disease due to its safe and effective profile (ATHENA trial),[14] although dronedarone is contraindicated in patients with NYHA III-IV or recently decompensated heart failure (ANDROMEDA trial),[15] where amiodarone should be used. Vernakalant is also mentioned as a drug recently approved which can be used for acute termination of recent-onset AF in patients with lone AF, AF associated with hypertension, stable coronary artery disease or mild to moderate heart failure.

When electrical or pharmacological cardioversion is decided, anticoagulation is considered mandatory: for AF < 48 h treatment with unfractionated heparin (UFH) or low-molecular weight heparin (LMWH), for AF of >48 h or AF of unknown duration, VKA treatment should be given for at least 3 weeks before cardioversion and a transesophageal echocardiogram should be performed to exclude left atrial (LA) or LA appenadage thrombus, spontaneous echo-contrast or complex aortic plaque. Recent guidelines are quite strict as far as anticoagulation is concerned, suggesting that VKA should be continued for a minimum of 4 weeks after cardioversion (due to 'atrial stunning') and life-long in patients with risk factors for stroke or AF recurrence.

In patients who remain symptomatic despite optimal medical therapy (including rate and rhythm control), catheter ablation should be reserved. It is clear that patients with heart failure benefit from AF ablation (e.g. improvement of ejection fraction/exercise tolerance) while no benefit has been demonstrated for asymptomatic patients. Another intervention included in recent guidelines is ablation of the atrioventricural node, a palliative and irreversible procedure that is reasonable when pharmacological rate control is not possible; selection of the appropriate cardiac implant depends on the type of AF and the presence/severity of associated heart disease (patients with reduced LV function may require biventricular pacing).

Finally, the 2010 guidelines introduced 'upstream therapy' to prevent or delay myocardial remodelling causing the development of AF (primary prevention) and reduce AF recurrence and progression to permanent AF (secondary prevention). Upstream therapy for AF includes treatment with angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), aldosterone antagonists, statins and omega-3 polyunsaturated fatty acids (PUFAs). In particular, ACEIs and ARBs are recommended for prevention of new-onset AF in patients with underlying heart disease (e.g. left ventricular hypertrophy, reduced ejection fraction) but evidence is less robust in secondary prevention. Statin therapy is reported to be effective in prevention of post-operative AF and more studies are required to define the role of aldosterone antagonists and PUFAs in prevention of AF.

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