ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΑΘΗΝΩΝ "Ο ΕΥΑΓΓΕΛΙΣΜΟΣ"
Α΄ ΚΑΡΔΙΟΛΟΓΙΚΟ ΤΜΗΜΑ

EVAGELISMOS GENERAL HOSPITAL OF ATHENS
A΄ DEPARTMENT OF CARDIOLOGY

April 2011 • Volume 6 • No 2 (22)

ISSN: 1792-7919 e-ISSN: 1792-7927

RHYTHMOS

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EDITORIAL

Discrepant Atrial Fibrillation Guidelines

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Recently, cardiological societies in Europe (ESC), US and Canada (CCS) have updated their guidelines for atrial fibrillation (AF). However, there are several discrepancies which have been identified and discussed. Among them, the following are the most blatant ones.

• **Anticoagulation.** Atrial fibrillation confers a 5-fold increase in the risk of stroke if left without anticoagulation therapy and a 2-fold increase in the risk of death from such thromboembolic strokes. The US guidelines recommend anticoagulation for a patient with a CHADS2 score of ≥2, and either aspirin or anticoagulation for a patient with a CHADS2 score of 1, while the CCS and ESC guidelines recommend anticoagulation for a patient with ≥1 risk factor(s). The new anticoagulants are taken into consideration by the CCS guidelines, recommending dabigatran instead of vitamin K antagonists (VKA). The ESC guidelines make recommendations for future use of dabigatran (when approved in the EU) depending on the risk of bleeding; for low-risk patients it may be considered, while for higher risk patients the lower dose of 110 mg of dabigatran may be considered. Also patients with a CHADS2 score of 1 may receive the lower dose (110 mg) of dabigatran. The US guidelines issued an update for dabigatran, indicating that it is a useful alternative to VKA. The FDA has approved only the higher dabigatran dose (150 mg bid) and a half-dose (75 mg bid) for patients with renal insufficiency. In the near future, the guidelines need also consider the newer anticoagulants, the active factor Xa inhibitors, rivaroxaban and apixaban, which are being tested in new randomized anticoagulation trials. Aspirin practically plays no role in thromboembolic prophylaxis in the ESC guidelines, but there is still a role in the US and CCS guidelines. The US and ECS guidelines recommend clopidogrel plus aspirin for patients who refuse warfarin therapy, while the CCS guidelines recommend dabigatran.

In an attempt for safer, more effective anticoagulation and to establish better risk profiles for assessing the likelihood of stroke in patients with AF by refining the use of CHADS2 score, the ESC guidelines introduced a new (deemed more sensitive) system called CHA2DS2-VASc, by adding in other risk factors. These include additional score points for specific age categories and for the presence of vascular disease and female gender. Furthermore, they linked to this a new score, HAS-BLED, for assessing bleeding risk.

• **Rate and Rhythm Control.** ESC guidelines recommend lenient *rate control* with a resting heart rate of <110 bpm (class IIa, level of evidence B) or stricter rate control for persisting symptoms or tachycardiomyopathy with a resting heart rate of < 80 bpm and heart rate during moderate exercise <110 bpm (also class IIa indication, level of evidence B). The US guidelines also accept

lenient heart rate control in patients with LVEF > 40%, but designate strict rate control as class III (of no benefit). In contrast, CCS guidelines recommend a target resting heart rate of <100 bpm.

Drugs to achieve *rate control* include beta-blockers, (non-hydropyridine) calcium blockers and digoxin. In addition, the ESC and CCS guidelines accept dronedarone for rate control in non-permanent AF (barring patients with NYHA III-IV or unstable heart failure); however, this needs to be proven in future studies. Amiodarone also constitutes second choice for rate control in both guidelines. The US guidelines do not provide recommendations for rate control. The CCS guidelines recommend atrio-ventricular (AV) junction ablation with implantation of a pacemaker for symptomatic patients with uncontrolled ventricular rates during AF despite maximally tolerated combined drug therapy. ESC guidelines recommend performing AV junction ablation in patients who are candidates for cardiac resynchronization therapy (CRT) or for CRT non-responders who are not paced in a biventricular mode due to fast AF.

For *rhythm control*, there is general agreement in the guidelines that the choice of antiarrhythmic therapy depends on the presence of underlying structural heart disease. Flecainide, propafenone and sotalol should be used only in patients with a structurally and functionally normal heart. Thus, amiodarone remains the sole relatively safe (less proarrhythmic) drug for use in patients with ischemic or non-ischemic cardiomyopathy with low ejection fraction. The US and ECS guidelines recommend avoidance of class IC antiarrhythmic drugs and sotalol in patients with left ventricular hypertrophy, while the CCS recommend avoidance of these drugs if there are repolarization abnormalities on the ECG.

All three guidelines included the new antiarrhythmic drug dronedarone, which was recently approved, into the recommendations. All agree that dronaderone should not be employed in patients with NYHA class III-IV or recently decompensated heart failure, per the results of the ANDROMEDA trial. However, there appear to be more problems with this new drug after market approval and more data are awaited for its safety. None of the guidelines make clear recommendations on the new atrial selective antiarrhythmic drug vernakalant, which has recently become available (intravenous form) for cardioversion of recent-onset AF; the ESC guidelines include it in a table and a footnote for future use for acute termination (pharmacological conversion) when approved.

• **Symptoms.** The ESC guidelines introduced a new symptom score for arrhythmias, the *EHRA score*, like the CCS class for angina or the NYHA class for heart failure. The EHRA score is designed to provide a classification of a patient's symptomatic status, for better and more specific treatment which is symptom-dependent.

• **Radiofrequency Ablation.** In all guidelines, ablation is generally reserved for symptomatic patients with paroxysmal lone AF (little or no structural heart disease), who have failed at least one trial of antiarrhythmic therapy. There are still some differences among the guidelines regarding this approach. The CCS guidelines consider the failure of ≥2 antiarrhythmic drugs as a strong recommendation for catheter ablation. The US guidelines recommend catheter ablation for patients with symptomatic paroxysmal AF who have failed an antiarrhythmic drug (class I indication, level of evidence A), when performed in experienced centers and in patients with normal or mildly dilated left atria, normal, or mildly reduced LV function and no severe pulmonary disease. The CCS and ESC guidelines make no mention of the left atrial size. Both the US and ESC guidelines distinguish between paroxysmal and persistent AF, whereas the CCS recommendations do not separate AF. The ESC guidelines consider catheter ablation for symptomatic AF after failure of an antiarrhythmic drug as class IIa indication (level of evidence A) and of persistent AF as IIa (level of evidence B). In patients with heart failure, ablation may be considered when antiarrhythmic therapy, amiodarone included, has failed (class IIb, level of evidence B).

In addition to the three categories of AF (paroxysmal - AF lasting <7 days; persistent AF -7 days to 1 year; and permanent AF), the ESC guidelines added another category, the long-standing persistent AF, defined as AF lasting > 1 year, creating a new category of patients felt to be candidate for ablation therapy.

• **Other Issues.** The ESC guidelines attempt to give advice on a number of "special situations", such as in athletes with AF, whereby drug treatment is often difficult, suggesting a pill-in-the pocket approach or ablation for more definitive therapy; also in patients with hypertophic cardiomyopathy, hyperthyroidism and pulmonary disease. The same guidelines provide recommendations on the so-called "upstream" therapy (use of ACE inhibitors, angiotensin-receptor blockers-ARBs, and statins), prescribed in an attempt to prevent the deterioration of AF. The CCS guidelines emphasize treatment of comorbidities such as hypertension and obstructive sleep apnea. Finally, a list of triggers and causes of AF are listed in Table 1.

Table 1. Causes, Triggers and Risk Factors for Atrial Fibrillation (AF)

Hypertension (esp. with associated LVH)
Diabetes
Ischemic heart disease
Cardiomyopathy (dilated and hypertrophic)
Heart Failure
Peri-myocarditis/pericardial effusion/constrictive pericarditis
Valvular heart disease
Congenital heart disease
Prior heart surgery
Bradyarrhythmias: sinus node dysfunction
Preexcitation syndromes / other supraventricular tachycardias / Atrial flutter
Thyroid disease
Chronic pulmonary disease
CVA
Obesity
Viral infections
Pneumonia
Pulmonary embolism
Sleep apnea
GI disorders
Sepsis
Electrolyte disturbances
Older age* / Race **
Alcohol, caffeine, nicotine
Drugs: beta-2 agonists, amphetamines, decongestants, xanthines, cocaine, glucocorticoids
Physical / emotional stress
Family history / genetic factors (mutations or single nucleotide polymorphisms)
Lone / idiopathic AF (5-10%)

CVA = cerebrovascular accident; GI = gastrointentistinal; LVH = left ventricular hypertrophy
* age-dependent / **more common in whites than in blacks ("AF paradox")

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