European Heart Journal (2013) **34**, 333–337
doi:10.1093/eurheartj/ehs451

REVIEW

The Year in Cardiology

The Year in Cardiology 2012: arrhythmia and pacing

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Received 11 November 2012; accepted 3 December 2012; online publish-ahead-of-print 2 January 2013

This paper was edited by Gerhard Hindricks, Herzzentrum Leipzig, Leipzig, Germany

This is a commissioned review for 'A Year in Cardiology 2012', focusing on recent developments in the field of arrhythmias and pacing.

Keywords Arrhythmias • Sudden death • Pacing • 2012

Atrial fibrillation

One of the most significant developments in terms of arrhythmia management in 2012 was the publication of the focused update of the ESC guidelines for the management of atrial fibrillation,[1] reviewing new evidence accumulated since the 2010 document and providing new recommendations in selected areas. A key change relates to a lowering of the threshold for the use of oral anticoagulant agents in patients with non-valvular AF, with anticoagulants recommended for all patients not identified as at a low risk on the basis of their CHA_2DS_2-VASc score (*Figure 1*). The exception to this recommendation is that female patients with gender alone as a single risk factor (still a CHA_2DS_2-VASc score of 1) would not need anticoagulation if they clearly fulfill the criteria of 'age $<$65 and lone AF'. In terms of the choice of oral anticoagulants, the document highlights 'better efficacy, safety and convenience' of the new agents (dabigatran, rivaroxaban, and apixaban) compared with warfarin, and suggests that their use should be considered for most patients with AF. With regard to interventional techniques for the left atrial appendage closure, the evidence of efficacy and safety in recent studies was considered insufficient to recommend these approaches for any patients other than those in whom long-term anticoagulation is contraindicated.

In terms of the use of specific antiarrhythmic agents for the maintenance of sinus rhythm, it is recommended that dronedarone should not be given to patients with moderate or severe heart failure, and should be avoided in patients with less severe heart failure if appropriate alternatives exist.

Catheter ablation of symptomatic paroxysmal AF after failed antiarrhythmic drug therapy was upgraded to a class 1 indication, provided the ablation is carried out by skilled operators. This is in line with the 2012 expert consensus statement on catheter and surgical ablation, co-authored by the EHRA.[2] Based on the results of recent randomized trials (e.g. MANTRA-PAF [3]), left atrial catheter ablation was considered 'reasonable' as first-line therapy in selected patients with paroxysmal AF and no structural heart disease. A randomized trial of adding left atrial cryoablation at the time of valve or coronary surgery revealed an increased incidence of sinus rhythm but with no demonstrable benefit in terms of morbidity or mortality at 1 year.[4]

The evidence for the use of oral anticoagulants to prevent embolic events associated with AF is based on patients with episodes of arrhythmia prolonged enough to be documented on 12-lead electrocardiograms. The increasingly widespread use of implantable devices with recording capabilities has raised the question of whether treatment is required for those with shorter episodes. In patients over 65 years, with implantable pacemakers or defibrillators, a history of hypertension and no history of clinical AF, subclinical episodes of AF lasting $>$6 min were found to be associated with a significantly increased risk of stroke or systemic embolism.[5] Randomized studies of anticoagulant therapy in such patients are now awaited.

Sudden death syndromes

Since the reported association of inferolateral early repolarization pattern and unexplained cardiac death in 2008, several groups have attempted to subclassify this common variant further so as to provide a useful clinical tool in the prediction of sudden death. A combination of J waves and horizontal/

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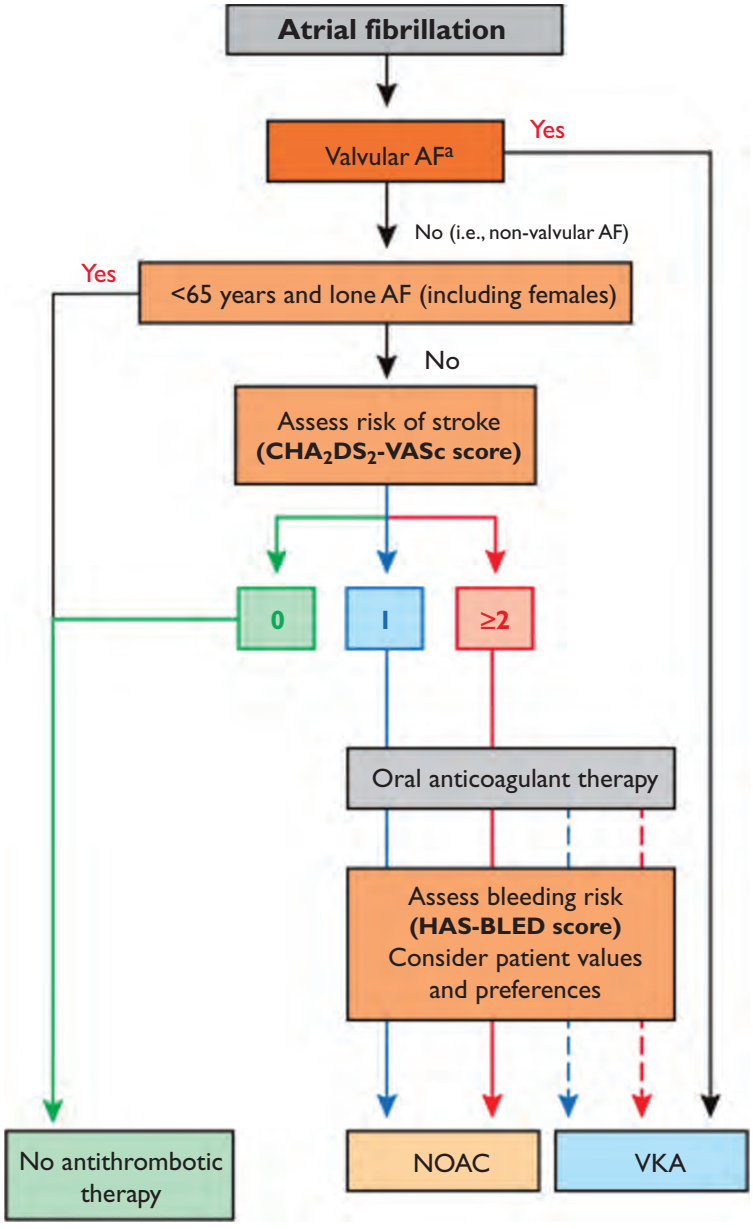

Antiplatelet therapy with aspirin plus clopidogrel, or—less effectively—aspirin only, should be considered in patients who refuse any OAC, or cannot tolerate anticoagulants for reasons unrelated to bleeding.If there are contraindications to OAC or antiplatelet therapy, left atrial appendage occlusion, closure or excision may be considered.
Colour: CHA_2DS_2-VASc; green = 0, blue = 1, red ≥2.
Line: solid = best option; dashed = alternative option.
AF = atrial fibrillation; CHA_2DS_2-VASc = see text; HAS-BLED = see text;
NOAC = novel oral anticoagulant; OAC = oral anticoagulant;
VKA = vitamin K antagonist.
[a]Includes rheumatic valvular disease and prosthetic valves.

Figure 1 Indications for oral anticoagulant (from Camm *et al.*[1]).

descending ST segment (as opposed to ascending) has been shown to increase the strength of this association[6] but not to the extent that it approaches clinical value as a predictive test. A large genome-wide association study has been unable to identify genetic variants associated with the pattern, possibly reflecting the phenotypic heterogeneity that exists among these individuals.[7]

One of the ultimate goals of genetic studies of patients with the congenital long QT syndromes is to determine reliable genetic markers of clinical risk. Despite nearly two decades of significant advance in terms of the underlying genetic causes of these syndromes, this goal has remained apparently distant, with standard individualized clinical risk markers (in particular presence or absence of a personal history of syncope and absolute length of the QT interval corrected for rate) conferring much greater prognostic power than 'genetic' risk factors. Barsheshet *et al.*[8] have provided data to show that within the cDNA sequence of the *KCNQ1* gene there are 44 amino acids (between residues 171–195 and 242–262) that, when replaced, confer a much higher risk of death than mutations in other regions of the gene, independently of clinical risk factors. These regions correspond to the cytoplasmic loops that group the two intracellular linkers between the transmembrane domain S2–S3 and S4–S5 in the predicted topology of the protein. The authors provide evidence to show that cytoplasmic loop mutations cause a decrease in adrenergic regulation of potassium channel function, associated with both higher risk and increased responsiveness to beta-blockade. Mutations in these regions are responsible for the condition in 7–15% of patients with LQT1.

There has been considerable controversy in recent years regarding risk assessment in patients with Brugada syndrome. This applies particularly to the role of programmed electrical stimulation in the selection of patients for defibrillator implantation. The Prelude registry of Brugada patients has recently reported[9] and has demonstrated convincingly that programmed electrical stimulation, irrespective of the number of premature beats used, is not predictive of arrhythmic events.

Another European study has reported predictors of malignant ventricular arrhythmias in patients with Lamin A/C mutations.[10] Eighteen per cent of a group of 263 mutation carriers followed for 43 months experienced malignant ventricular arrhythmias. Independent risk factors for these events were non-sustained ventricular tachycardia, ejection fraction $<45\%$, male sex, and non-missense mutations. Malignant arrhythmias occurred only in individuals with at least two of these risk factors.

Sudden death during athletic activity is an emotive if rare event.[11] Long distance races are known to be associated with cardiac dysfunction, although with a low overall risk of cardiac arrest and sudden death. A large American study[12] showed that cardiac arrest occurs primarily among male marathon participants and is most commonly attributable to hypertrophic cardiomyopathy or atherosclerotic coronary artery disease. Post-mortem studies suggested that the mechanism of cardiac arrest associated with coronary disease appeared to be the mismatch between oxygen supply and demand rather than plaque rupture.

Wolff-Parkinson-White syndrome

The management of a young asymptomatic patient with Wolff-Parkinson-White syndrome is often contentious. A recent PACES/HRS consensus statement suggests that in 8–21 year olds if pre-excitation cannot be shown to be intermittent by ambulatory ECG or exercise test, then transoesophageal or intracardiac EP studies should be performed, and ablation discussed with those in whom the shortest RR interval during induced AF is <250 ms.[13]

Innovations in electrophysiological testing/ablation

This year saw the publication of early 'proof of principle' studies on the use of real-time magnetic resonance imaging to guide catheter positioning during electrophysiological studies and catheter ablation procedures.[14,15]

Cardiac resynchronization therapy

2012 saw the publication of the EHRA expert consensus statement on cardiac resynchronization therapy (CRT) in heart failure.[16] This document aims to advise the implanting physician on issues regarding CRT patient care, and is intended to provide the evidence base to help physicians maximize response to therapy acutely and chronically. Particular emphasis is given to problem solving in specific populations including the 'non-responders' to therapy.

A study by Dupont *et al.*[17] has emphasized the importance of left bundle branch morphology in the prediction of a beneficial response to CRT. Patients with a shorter QRS (120–149ms) but left bundle branch block (LBBB) morphology still had a better clinical response than patients with QRS duration over 150 ms but non-LBBB morphology. A systematic review of studies of patients undergoing CRT with both AF and symptomatic heart failure[18] has indicated that AV nodal ablation in such patients with poor rate control results in a reduction in mortality and improvements in functional class compared with medical therapy.

Subcutaneous implantable cardioverter defibrillator

In September 2012 The US Food and Drug Administration granted Boston Scientific Corporation regulatory approval for its S-implantable cardioverter defibrillator (ICD)® System, the subcutaneous implantable defibrillator. Approval of the system was based on data from a 330-patient, prospective, non-randomized, multicentre clinical study, which evaluated the safety and effectiveness of the system in patients at risk of sudden cardiac arrest and was presented earlier this year at the Heart Rhythm Society 33rd Annual Scientific Sessions.[19] The subcutaneous ICD was initially developed for patients who were not candidates for transvenous ICDs such as those with congenital heart abnormalities or no venous access. Although the device has been demonstrated to identify and treat ventricular arrhythmias accurately and effectively, the absence of any pacing ability (other than immediately post-shock) excludes its use for several important clinical therapies,

including back-up pacing for bradycardias, resynchronization therapy for heart failure, and antitachycardia pacing. Nevertheless, the majority of patients requiring an ICD will likely be candidates for either a subcutaneous or a transvenous device and the largest determinant of device selection in the medium term is likely to be clinician preference and experience, with a preference for the transvenous approach at present given the relatively small number of physicians trained in the subcutaneous technique and the fact that long-term efficacy and safety data continue to be acquired.[20,21]

Riata leads

Approximately 227 000 Riata and Riata ST ICD leads had been sold worldwide when they were removed from the market by St Jude Medical in December 2010, following the discovery of externalized conductors consequent upon 'inside-out" abrasions against the relatively soft silicone rubber insulation. The scale and significance of this problem has become clearer in 2012. It now seems that externalized conductors are just one of a number of consequences of the silicone rubber disruption. Depending upon the site of insulation failure, bare cable conductors can come in contact with the shocking coil or can, leading to shorting and failure of defibrillation shocks.[22]

Device longevity

While there have been many advances in pacemaker and defibrillator technology over the past decades, it could be argued that developments have focused more on improving diagnostic/therapeutic capabilities and reducing size rather than improving battery longevity. Thijssen *et al.*[23] have examined predictors of ICD longevity in a clinical population encompassing devices from several manufacturers. Overall, devices lasted an average of 5 years before battery depletion. Devices implanted after 2002 lasted ~6 months longer than those implanted before 2002. In general, devices implanted by Medtronic lasted the longest, followed by Guidant, with the shortest longevity in St Jude and Biotronik devices. Early studies of 'piezoelectric energy harvesting' have shown potential to supplement battery power and improve longevity in the future.[24]

Pacing for neurally mediated syncope

The intuitively attractive treatment of permanent pacing for neurally mediated syncope has not, in the past, fared well under the spotlight of randomized controlled trials. The Third International Study on Syncope of Uncertain Etiology (ISSUE-3)[25] examined the role of pacing in the subset of patients with recurrent syncope and pauses of >3 s documented with implantable loop recorders at the time of syncope. In this small study of 77 patients, pacing resulted in a statistically significant reduction in syncope recurrence, giving support for the use of this therapy in this selected group of individuals.

Conflict of interest: none declared.

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