FEATURE

European Heart Rhythm Association Scientific Documents Reports

Written by Toni Rizzo

The European Heart Rhythm Association (EHRA) scientific documents provide advice based on scientific data in emerging areas of arrhythmia management in Europe. The documents contain advice rather than guidelines because insufficient evidence exists to develop specific recommendations in these areas.

LEFT ATRIAL APPENDAGE OCCLUSION FOR ATRIAL FIBRILLATION

Michael Glikson, MD, Chaim Sheba Medical Center, Tel Hashomer, Israel, presented draft findings of the EHRA and European Association of Percutaneous Cardiovascular Interventions (EAPCI) Scientific Document Committee on the European Cardiac Resynchronization Therapy Survey: comparison of outcomes between de novo cardiac resynchronization therapy implantations and upgrades (LAAO) for atrial fibrillation (AF).

Table 1 summarizes the committee's findings on the standards and requirements, devices, imaging, and data collection and registries for LAAO in patients with AF.

Oral anticoagulants remain the standard for first-line treatment of AF. New oral anticoagulants (NOACs) are preferred for patients with excessive risk of anticoagulation. LAAO has not been compared with NOACs in clinical trials. However, the risk of bleeding with some NOACs, including low dose dabigatran and apixaban, is expected to be lower than with warfarin.

LAAO should be considered for patients with an unacceptable risk of bleeding with oral anticoagulation, who refuse oral anticoagulation, or those with contraindications for any oral anticoagulation (Figure 1). The committee found no evidence to support LAAO as an adjunct to oral anticoagulants or AF ablation. Prof. Glikson concluded that future randomized controlled trials are needed to provide evidence for the use of LAAO in patients with AF, particularly to study the Amplatzer Cardiac Plug device, high-risk populations with contraindications to oral anticoagulants, LAAO versus NOACs, future devices, and epicardial approaches.

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Figure 1. Indications for Left Atrial Appendage Occlusion

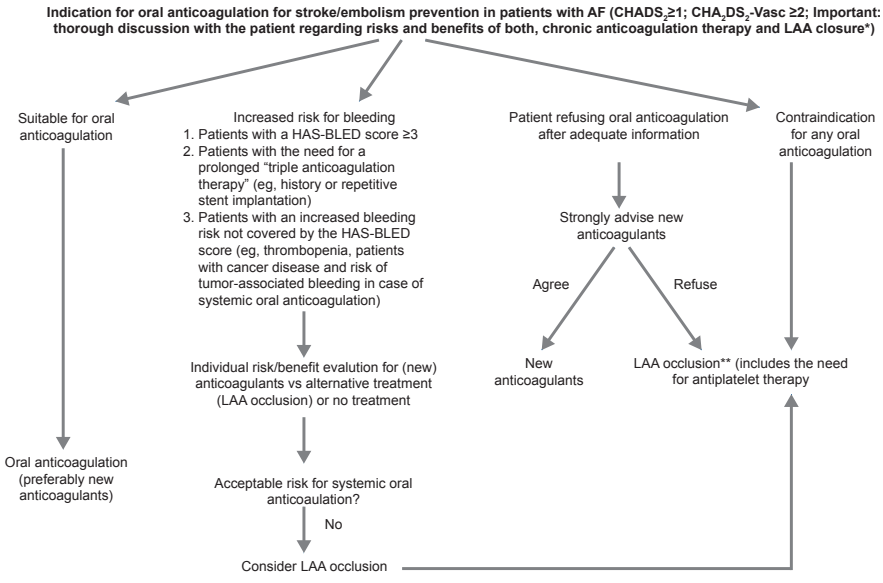


Table 1. Scientific Document Committee Findings for LAAO for AF

Topic	Evidence
Standards and requirements	▪ Operator acquainted with transseptal techniques and LAA anatomy, and must: » Attend live cases in training hospitals » Be proctored for several cases at home institution ▪ Experienced echocardiographer ▪ Available surgical back-up ▪ Experience with pericardiocentesis
Devices	▪ Watchman and ACP most commonly used
Watchman	▪ Approximately 1400 implanted ▪ PROTECT AF randomized trial [Holmes DR et al. *Lancet* 2009], CAP Registry [Reddy VY et al. *Circulation* 2011; NCT00129545], ASAP registry [NCT00851578; Reddy VY et al. *Heart Rhythm* 2012], PREVAIL randomized trial [NCT01182441] ▪ Successful implantation rates, 88% to 95% ▪ Efficacy event rates, 1.07% to 2.3% per 100 patient-years ▪ Safety event rates, 3.6% to 8.7%
ACP	▪ Approximately 700 implanted ▪ Italian Registry, Dual Centre, ACP EU Post-Market Registry [Park JW. CSI 2011], Initial European Experience [Park JW, et al. *Catheter Cardiovasc Interv* 2011], Bern LAAO Registry, LAAO With ACP trial [Urena M et al. *J Am Coll Cardiol* 2013] ▪ Technical success rates, 96% to 100% ▪ Adverse event rates, 0.8% to 7.6%
Imaging	▪ Gold standard is TEE ▪ CTA (before procedure), MRA, and ICE are potential alternatives
Before procedure	▪ Exclude LAA thrombus ▪ Measure diameter and length of LAA in several angles to determine appropriate device
During procedure	▪ Guide transseptal puncture for safety and to locate it posterior and inferior to usual location ▪ Use with fluoroscopy to locate device within appendage ▪ Look for leaks ▪ Monitor for complications
After procedure	▪ Perform at 6 weeks, 6 months, and 1 year after procedure using protocol from PROTECT AF trial [Holmes DR et al. *Lancet* 2009] ▪ Look for thrombus ▪ Verify absence of leaks <5 mm ▪ Ensure device is not dislodged ▪ Guide anticoagulation
Data collection and registries	▪ Demographic data ▪ Type of device ▪ Type of AF ▪ Cardiovascular history ▪ $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED scores ▪ Antithrombotic therapy prior to procedure and at discharge ▪ Indication for implantation ▪ Type and size of device ▪ Complications ▪ Clinical and echocardiographic follow-up at 6 weeks, then yearly, including: » Mortality » Cardiovascular accident » Device embolization » Bleeding » Leaks
Indications	▪ ESC 2012 recommendation for LAAO » The only existing guideline for LAAO » Recommends LAAO in patients with high stroke risk and contraindications for long-term oral anticoagulation [Camm AJ et al. *Eur Heart J* 2012] » No randomized controlled trials on LAAO in patients with contraindications to anticoagulants

ACP=amplatzer cardiac plug; AF=atrial fibrillation; CTA=computed tomography angiography; ESC=European Society of Cardiology; ICE=intracardiac echocardiography; LAA=left atrial appendage; LAAO=left atrial appendage occlusion; MRA=magnetic resonance angiogram; TEE=transesophageal echocardiogram.

NEW ORAL ANTICOAGULANTS – PRACTICAL ADVICE FOR DIFFICULT SITUATIONS

The EHRA has developed a practical guide for the use of NOACs in patients with nonvalvular AF [Heidbuchel H et al. *Europace* 2013]. Lead author, Hein Heidbuchel, MD, PhD, University of Leuven, Leuven, Belgium, said that the intent of the guide is to inform physicians on how to use these drugs safely and effectively in clinical practice. The guide addresses the four NOACs: dabigatran, rivaroxaban, apixaban, and edoxaban. All but edoxaban are approved by the European Medicines Agency; edoxaban currently is under investigation in the ENGAGE-AF trial [NCT00781391], with results expected at the American Heart Association (AHA) 2013 meeting. An associated Web site, www.NOACforAF.eu, complements the published guide, including patient anticoagulation cards, feedback forms, a slide kit, a key messages pocket guide, and updates.

The EHRA guide provides a practical start-up and follow-up scheme for physicians to use when prescribing NOACs. Detailed information on absorption and metabolism

of NOACs is provided (Table 2) as well as an overview of potential drug-drug interactions and comorbidities which may require dosing considerations. The guide also discusses on how to manage dosing errors.

Table 2. Absorption and Metabolism of NOACs

	Dabigatran	Apixaban	Edoxaban*	Rivaroxaban
Bioavailability	3%-7%	50%	62%	66% (w/o food) ~100% (with food)
Prodrug	yes	no	no	no
Clearance: non-renal/ renal **of absorbed** dose if normal renal function	20%/80%	73%/27%	50%/50%	65%/35%
Liver metabolism: CYP3A4	no	yes (elimination; minor CYP3A4)	minimal (<4% of elimination)	yes (elimination)
Absorption with food	no effect	no effect	6%-22% more	+39%
Intake with food?	no	no	no official recommendation yet	mandatory
Absorption with H2B/PPI	plasma level -12 to -30%	no effect	no effect	no effect
Asian ethnicity	plasma level +25%	no effect	no effect	no effect
GI tolerability	dyspepsia 5%-10%	no problem	no problem	no problem
Elimination half-life	12-17h	12h	9-11h	5-9h (young)/ 11-13h (elderly)

NOAC=new oral anticoagulant.

The guide includes detailed tables on cessation before planned and urgent surgery, bleeding complications, and use of coagulation assays with the NOACs.

The use of NOACs in patients with AF and coronary artery disease, kidney disease, and those undergoing ablation or cardioversion, as well as management of patients with acute stroke or acute coronary syndrome while on NOACs are also addressed. Although scientific evidence is lacking for some of these issues, updated information will be provided on the EHRA website (www.NOACforAF.eu) as data become available.

HEART IMAGING IN PATIENTS UNDERGOING ABLATION

The EHRA consensus statement on imaging for electrophysiological and device procedures was developed at the first EHRA Policy Conference [Lundqvist CB et al. *Europace* 2013]. According to lead author Carina Blomström Lundqvist, MD, PhD, Uppsala University, Uppsala, Sweden, the objective of the Policy Conference was to assess the state of evidence and possibility for formal recommendations on the development and use of new imaging tools in electrophysiology and device implantation (Table 3).

Table 3. Imaging Requirements and Uses

Setting	Imaging Modality	Uses and Minimum Requirements
Before ablation	Chest x-ray	Individual indication
	Echocardiography	Image anatomy, LV function, underlying disease No radiation, low cost, ready availability, rapid
	Transthoracic	LV function LA size Mitral valve function LV hypertrophy Required for all patients
	Transesophageal	Exclude LA thrombus Required for all patients
	MRI and CT	Image difficult anatomy (cavotricuspid isthmus, coronary sinus, superior vena cava, pulmonary vein) Risk stratification based on location and extent of atrial fibrosis (MRI, investigational technique) Requirement depends on ablation method used
	Coronary angiography	Assess coronary and peripheral artery disease Individual indication
	Vascular ultrasound	Assess peripheral artery disease
During ablation	Echocardiography	Assess complications such as tamponade Optional
	Transthoracic	Assess complications
	Transesophageal	Detect transseptal puncture
	Intracardiac	Catheter visualization
	Fluoroscopy	Catheter visualization, mapping, ablation Pulmonary vein angiography Detect tamponade Required
	Rotation angiography Nonfluoroscopic navigation systems including intracardiac echocardiography	Optional Catheter positioning Image specific anatomic structure Required
	Vascular ultrasound	Assess complications of peripheral arteries
After ablation (all optional)	Echocardiography	Assess complications Evaluate effect on cardiac function
	Transthoracic	Pulmonary embolism, tamponade
	Transesophageal	Pulmonary vein stenosis, stroke
	Vascular sonography	Assess complications (ie, bleeding and aneurysm)
	MRI and CT	Pulmonary vein stenosis Esophageal injury Assess extent and location of ablation lesion (MRI, not routine)

CT=computed tomography; LA=left atrium; LV=left ventricle; MRI=magnetic resonance imaging.

The Policy Conference brought together experts in the areas of radiology, electrophysiology, and cardiac imaging to assess the evidence and develop a guide for heart imaging in patients undergoing ablation. The resulting document is a key step in guiding the future clinical use of these technologies.

ELECTROPHYSIOLOGICAL PROCEDURES IN CHILDREN

Josep Brugada Terradellas, MD, PhD, University of Barcelona, Barcelona, Spain, presented the EHRA/Association for European Pediatric Cardiology (AEPC) consensus document titled Pharmacological and Non-Pharmacological Therapy for Arrhythmias in the Pediatric Population, focusing on electrophysiological procedures in children [Not yet published].

Device implantation in children is a challenge, requiring the use of both the transvenous and epicardial routes. The technique used depends on the size of the patient, underlying anatomy, venous patency, and experience of the unit. Complications are more frequent in children than in adults.

According to Prof. Brugada, pediatric catheter ablation should be performed in specialized centers by electrophysiologists experienced in pediatric ablations in collaboration with pediatric cardiologists. Three-dimensional mapping and nonfluoroscopic navigation is required for ablation of complex arrhythmias such as those associated with congenital heart disease. While ablation can be performed in older children under conscious or deep sedation, most patients aged <10 years require general anesthesia. Modifications of the ablation procedure may be needed in small children to avoid complications, including use of 5F radiofrequency ablation catheters and single diagnostic electrophysiological catheters. Lower power and temperature settings may reduce the risk of coronary and myocardial injury. Indications for pediatric catheter ablation are shown in Table 4.

Prof. Brugada emphasized that individual decision making is of "utmost importance," especially in young children. Antiarrhythmic drug therapy can be effective and may be preferable in certain situations, particularly in younger children.

Table 4. Indications for Pediatric Catheter Ablation

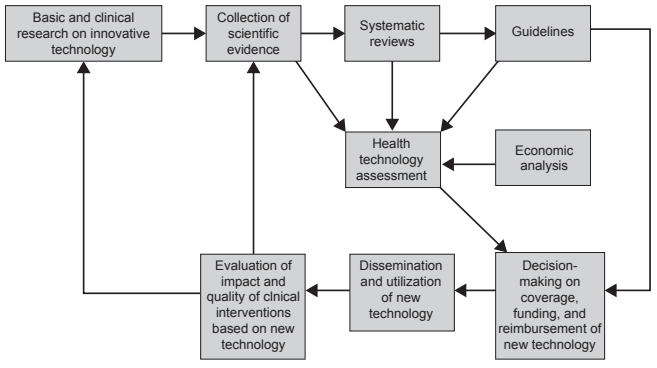
Clinical Situation	Class	Level
WPW and episode of aborted sudden cardiac death	I	C
WPW syndrome and syncope, preexcited RR <250 ms	I	C
WPW and recurrent SVT and age >5 years	I	C
WPW and recurrent SVT and age <5 years	IIb	C
WPW and palpitations with inducible SVT, age >5 years	I	C
Asymptomatic preexcitation, age >5 years, no tachycardia	IIb	C
Asymptomatic preexcitation, age <5 years	III	C
Incessant or recurrent SVT and ventricular dysfunction	I	C
Monomorphic VT and hemodynamic compromise	I	C
Single or infrequent SVT (no preexcitation), age >5 years	IIb	C
SVT, age >5 years, AAD effective	IIa	C
SVT, age <5 years, AAD not effective or with side effects	IIa	C
SVT controlled with conventional AAD, age <5 years	III	C

AAD=antiarrhythmic drugs; SVT=supraventricular tachycardia; VT=ventricular tachycardia WPW=Wolff-Parkinson-White.

HEALTH TECHNOLOGY ASSESSMENT FOR ELECTROPHYSIOLOGICAL PROCEDURES

The Health Technology Assessment in Interventional Electrophysiology and Device Therapy: A Position Paper of the EHRA [Boriani G et al. *Eur Heart J* 2013] was presented by Giuseppe Boriani, MD, PhD, University of Bologna, Bologna, Italy. Health technology assessments (HTAs) are conducted by a multidisciplinary team to evaluate the clinical- and cost-effectiveness of healthcare interventions. Factors considered in an HTA include quality, safety, efficacy, cost, cost-effectiveness, and organizational, legal, and social aspects. The EHRA HTA process is outlined in Figure 2.

Figure 2. Health Technology Assessment Process



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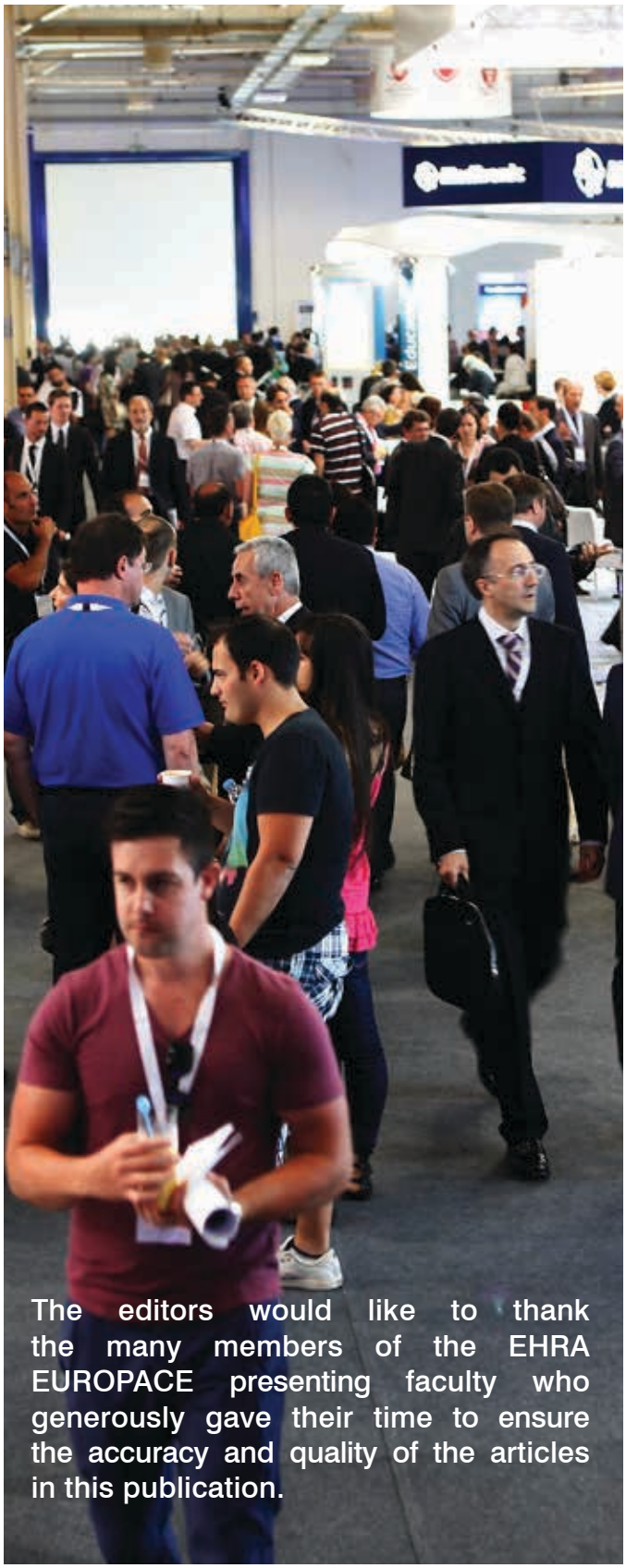
The benefits of electrophysiological interventions include prolonging life, preventing cardiovascular death and stroke, improving exercise capacity and quality of life, preventing symptoms of arrhythmia and hospitalizations, and improving social and cognitive functioning. However, economic pressures may limit availability of devices with a high upfront cost, such as implantable cardioverter-defibrillators. HTAs employ an economic analysis, including cost-effectiveness, cost-utility, and cost-benefit, rather than a financial analysis that considers only cost.

The EHRA recommendations for HTAs in interventional electrophysiology and device therapy are summarized in Table 5.

Table 5. Recommendations for Undertaking Economic Evaluations in Interventional Electrophysiology and Device Therapy

	Recommendations
Questions and study population	▪ Address questions relevant to patient groups in which clinical effectiveness has been proved ▪ Undertake separate appraisal of inappropriate or suboptimal use of interventions
Outcomes	▪ Mortality and other cardiology outcomes should be main basis for HTA evaluations ▪ Quality-adjusted life-years are preferred summative measure of clinical outcome
Costs	▪ Based on resources and subdivided direct healthcare and non-healthcare costs
Economic evaluation	▪ Adopt a lifetime horizon in economic evaluations of therapies for chronic conditions ▪ Clinical data from trials can be used to reflect the average expected duration of the interventional effect
Budget impact, organizational, and educational issues	▪ Present budget impact of a therapy in terms of upfront costs and overall cost over duration of therapy ▪ Address issues related to training, education, and definition of appropriate setting for therapy

Prof. Boriani cautioned against getting caught in the "innovation paradox," in which older or cheaper products are bought to cut costs, resulting in reduced quality and service, and ultimately, a decline in productivity and efficiency. Instead it is important to embrace innovation by investing in optimizing healthcare delivery to patients to achieve health outcomes and quality goals, resulting in improved productivity and efficiency.



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