

Key messages to comprehend: The European Heart Rhythm Association (EHRA) consensus document - How to manage device-detected subclinical atrial tachyarrhythmias

Emin Evren Ozcan¹, Gulmira Kudaiberdieva², Bulent Gorenek^{2,3}

¹Dokuz Eylul University, Department of Cardiology, Izmir

²Heart Vessels and Transplantation

³Eskisehir Osmangazi University, Department of Cardiology, Eskisehir, Turkey

Atrial fibrillation (AF) is the most common sustained arrhythmia. In the last 20 years, it has become one of the most important public health problems and a significant cause of increasing healthcare expenditures. The prevalence of AF is also increasing due to the improved ability to suspect and diagnose AF in the setting of variety of chronic cardiac and non-cardiac diseases.

Actually, we know much about management of AF in symptomatic patients. However, many patients with AF are asymptomatic. Silent AF is far more frequent than symptomatic AF in patients with paroxysmal AF. Moreover, both clinical and silent AF, are associated with an increased risk of thromboembolism. With advancement in technology and widespread use of cardiac devices, subclinical atrial tachyarrhythmias (AT) are becoming more visible. Although device-detected subclinical ATs are frequently encountered in daily practice, management of them is not addressed by current guidelines. Physicians need expert recommendations to guide management of these tachyarrhythmias.

European Heart Rhythm Association, recently published a consensus document that address clinical management of device-detected subclinical AT with representation from the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS) and Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología (SOLEACE) (1). We provide here the key messages from document conceptualized by specialist dealing with such problems in daily practice.

Consensus document firstly reviews the detection properties of cardiac devices. It underlines the advantage of cardiac electronic devices to detect subclinical atrial fibrillation (SCAF). Patients with cardiac implanted electronic devices (CIEDs) have an advantage over patients who do not have implanted

device because clinically silent arrhythmias can be detected. In addition, remote monitoring can also provide earlier detection compared to standard scheduled follow-up.

Besides these advantages, even in automatic detection of AF by devices, false positive and false negative detections may lead to misinterpretation of stored data. Therefore, consensus document recommends the implantation of a bipolar atrial lead for reliable AF detection if it is indicated. High atrial sensitivity is also crucial to avoid intermittent undersensing of AF. Most importantly, review of stored intracardiac electrograms to confirm diagnosis and exclude artifact or reduce the effect of oversensing/undersensing by automated algorithms is recommended by the document.

In high-risk patients who have no CIEDs, noninvasive monitoring may be considered for detection of SCAF. The 24-hour Holter monitor is the most established but least sensitive device for continuous ECG monitoring. Other devices with longer monitoring periods (e.g. longer term Holter monitoring and event recorders) are associated with a greater rate of SCAF detection. However, the cost of the methods is also increasing.

Implantable loop recorders (ILR) are invasive systems that provide very long monitoring period. Continuous arrhythmia monitoring up to 1-year in patients with cryptogenic stroke detects AF with prevalence of 20% (2). However, the topography (shape, size and location) of the cerebral ischemic infarction area is not related to AF prevalence (3). Although they can be used for AF detection after cryptogenic stroke, this strategy has not been shown to have clinical utility in regard to future stroke prevention (4). In the consensus report, it is stated that implantation of ILR may be limited in patients with cryptogenic stroke other than clinical research subjects. The need of comparative studies on

Address for Correspondence: Bulent Gorenek,

Department of Cardiology, Eskisehir Osmangazi University, Medical Faculty, Meselik, Eskisehir, Turkey

E-mail: bulent@gorenek.com Received: 29.10.2017 Accepted: 30.10.2017

Copyright© 2017 Heart Vessels and Transplantation

these various external devices and cost-effectiveness analyses on the use of these devices is also reported. Inexpensive and noninvasive tools like smartphone ECG applications are offered for screening of SCAFs, especially in patients with ischemic stroke or TIA without a history of AF.

After review of detection methods, uncertainties in pathophysiologic link between device detected AT and thromboembolic risk is discussed.

All major studies regarding the thromboembolic risk of SCAF in patients with CIEDs show significant increases in stroke rate associated with device-detected atrial high rate episodes (AHRE) (5-11). However, the minimum duration of episode or AT/AF burden (longest total duration of AF on any given day), which confers increased thromboembolic risk is not precisely defined. The minimum duration of device-detected AF that increases thromboembolic risk is not certain, it may be as brief as 5 minutes to several hours.

Temporal association between AHREs and the occurrence of stroke is also not clear. Related studies revealed unexpected findings; there was no AF on the device recordings in the majority of patients (73-94%) in the 30 days prior to the thromboembolic events (4,11-13). These findings suggest that the mechanism of stroke may not be related to the AF episodes. AHRE could simply be a risk marker for stroke, or reflect an indirect mechanism related to multiple comorbidities associated with stroke.

Consensus document cites the recent studies focusing on fibrotic atrial cardiomyopathy and thromboembolism have led to a new paradigm of understanding the mechanism of stroke. AF may not be a direct causal, but it may be marker and an amplifier of underlying atrial pathology (14,15).

The authors also remind the risk of excessive supraventricular ectopic activity (ESVEA) associated with risk of incident AF, stroke and mortality (16,17). They note that excessive supraventricular ectopic activities documented by Holter monitoring can be considered be a surrogate marker for paroxysmal AF.

At the end of the document authors, make valuable recommendations for daily practice, especially for oral anticoagulation therapy. First, they emphasize that the symptoms are not decisive instruments determining the need for anticoagulation.

For patients with two additional CHA₂DS₂-VASc risk factors (ie. ≥ 2 in males, ≥ 3 in females) oral anticoagulation is recommended for AF burden >5.5 h/day. Nevertheless, it should be kept in mind that the minimum duration of AHRE that increases thromboembolic risk is not certain. Therefore, lower duration may merit oral anticoagulation if multiple risk factors are present. At the same time, it is reasonable to follow-up a patient with only a single 5- min episode to observe their

AF burden over time before committing them to life-long oral anticoagulation.

Consensus document suggest to consider oral anticoagulation for AF burden of >5.5 h in patients with one additional CHA₂DS₂-VASc risk factor and not to start antithrombotic therapy for any patient with CHA₂DS₂-VASc score of 0 irrespective of AHRE.

This well-prepared document comprehensively reviews the pathophysiologic link between device-detected SCAF and stroke. It answers many daily clinical questions for management of SCAF and treatment with oral anticoagulation.

Peer-review: Internal.

Conflict of interest: None to declare.

Authorship: E.E.O, G.K. and B.G equally contributed to the preparation of manuscript.

Acknowledgement and funding: None to declare.

References

- Gorenk B, Bax J, Boriani G, Chen SA, Dagnes N, Glotzer TV, Healey JS, Israel CW, Kudaiberdieva G, Levin LA, Lip GYH, Martin D, Okumura K, Svendsen JH, Tse HF, Botto GL. Device-detected subclinical atrial tachyarrhythmias: definition, implications and management—an European Heart Rhythm Association (EHRA) consensus document, endorsed by Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS) and Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología (SOLEACE). *Europace* 2017; 19: 1556-78.
- Afzal MR, Gunda S, Waheed S, Sehar N, Maybrook RJ, Dawn B, et al. Role of outpatient cardiac rhythm monitoring in cryptogenic stroke: a systematic review and meta-analysis. *Pacing Clin Electrophysiol* 2015; 38: 1236-45.
- Li L, Yiin GS, Geraghty OC, Schulz UG, Kuker W, Mehta Z et al.; Oxford Vascular Study. Incidence, outcome, risk factors, and long-term prognosis of cryptogenic transient ischaemic attack and ischaemic stroke: a population-based study. *Lancet Neurol* 2015; 14: 903-13.
- Martin DT, Bersohn B, Waldo AL, Wathen MS, Choucair WK, Lip GY, et al. Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and resynchronization devices. *Eur Heart J* 2015; 36: 1660-8.
- Glotzer TV, Hellkamp AS, Zimmerman J, Sweeney MO, Yee R, Marinchak R, et al.; MOST Investigators. Atrial high rate episodes detected by pacemaker diagnostics predict death and stroke: report of the Atrial Diagnostics Ancillary Study of the MOde Selection Trial (MOST). *Circulation* 2003; 107: 1614-9.
- Healey JS, Connolly SJ, Gold MR, Israel CW, Van Gelder IC, Capucci A, et al.; ASSERT Investigators. Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med* 2012; 366: 120-9.
- Capucci A, Santini M, Padeletti L, Gulizia M, Botto G, Boriani G, et al. Monitored atrial fibrillation duration predicts arterial embolic events in patients suffering from bradycardia and atrial fibrillation implanted with antitachycardia pacemakers. *J Am Coll Cardiol* 2005; 46: 1913-20.
- Botto GL, Padeletti L, Santini M, Cappucci A, Pulizia M, Zolezzi F et al. Presence and duration of atrial fibrillation detected by continuous monitoring: crucial implications for the risk of thromboembolic events. *J Cardiovasc Electrophysiol* 2009; 20: 241-8.
- Glotzer TV, Daoud EG, Wyse DG, Singer DE, Ezekowitz MD, Hilker C, et al. The relationship between daily atrial tachyarrhythmia burden from implantable device diagnostics and stroke risk: the TRENDS study. *Circ Arrhythm Electrophysiol* 2009; 2: 474-80.

10. Shanmugam N, Boerdlein A, Proff J, Ong P, Valencia O, Maier SK, et al. Detection of atrial high-rate events by continuous home monitoring: clinical significance in the heart failure-cardiac resynchronization therapy population. *Europace* 2012; 14: 230-7.
11. Boriani G, Glotzer TV, Santini M, West TM, De Melis M, Sepsi M, et al. Device-detected atrial fibrillation and risk for stroke: an analysis of > 10,000 patients from the SOS AF project (Stroke preventiOn Strategies based on Atrial Fibrillation information from implanted devices). *Eur Heart J* 2014; 35: 508-16.
12. Daoud EG, Glotzer TV, Wyse DG, Ezekowitz MD, Hilker C, Koehler J, et al.; TRENDS Investigators. Temporal relationship of atrial tachyarrhythmias, cerebrovascular events, and systemic emboli based on stored device data: a subgroup analysis of TRENDS. *Heart Rhythm* 2011; 8: 1416-23.
13. Brambatti M, Connolly SJ, Gold MR, Morillo CA, Capucci A, Muto C, et al.; ASSERT Investigators. Temporal relationship between subclinical atrial fibrillation and embolic events. *Circulation* 2014; 129: 2094-9.
14. Hirsh BJ, Copeland-Halperin RS, Halperin JL. Fibrotic atrial cardiomyopathy, atrial fibrillation, and thromboembolism: mechanistic links and clinical inferences. *J Am Coll Cardiol* 2015; 65: 2239-51.
15. Kamel H, Okin PM, Elkind MS, Iadecola C. Atrial Fibrillation and mechanisms of stroke: time for a new model. *Stroke* 2016; 47: 895-900.
16. Binici Z, Intzilakis T, Nielsen OW, Køber L, Sajadieh A. Excessive supraventricular ectopic activity and increased risk of atrial fibrillation and stroke. *Circulation* 2010; 121: 1904-11.
17. Larsen BS, Kumarathurai P, Falkenberg J, Nielsen OW, Sajadieh A. Excessive atrial ectopy and short atrial runs increase the risk of stroke beyond incident atrial fibrillation. *J Am Coll Cardiol* 2015; 66: 232-41.