



Letters to the Editor

Corundum of stroke risk in atrial high rate episodes



Dear Editor,

We have read with great interest the article by Nakano et al. investigating the impact of atrial high-rate episodes (AHRE) on the risk of embolic stroke [1]. Similar to previous major studies, the authors demonstrated significant increases in embolic stroke rate associated with device-detected AHRE. However, the minimum duration of episodes that increase the thromboembolic risk is variable in all these studies.

According to the recent consensus document of the European Heart Rhythm Association regarding device-detected subclinical atrial tachyarrhythmias, oral anticoagulation is recommended for atrial fibrillation (AF) burden >5.5 h/day for patients with two additional CHA₂DS₂-VASc risk factors (i.e. ≥ 2 in males and ≥ 3 in females) [2].

In addition to this recommendation, Gorenek et al. underline the challenges of determining definite minimum episode duration to initiate anticoagulation therapy [2,3].

Nakano et al. provide valuable data regarding this association. The authors report that 30 s is the best cut-off time of AHRE detected by cardiac implantable electronic devices for predicting the risk of embolic stroke in a population that had no history of AF. However, the existence of temporal relationship between AHREs and the occurrence of stroke was not evaluated in this study.

Previous studies revealed confounding results. In the majority of patients there was no AHRE in the 30 days prior to the thromboembolic events [2,4]. These findings suggest that the mechanism of stroke may not be related to the AHRE. They may reflect an indirect mechanism related to multiple comorbidities associated with stroke. Nakano et al. have the data supporting this possibility. In this study, patients with AHRE had significantly higher CHADS₂ and CHA₂DS₂-VASc scores than those without episodes of AF (2.0 ± 1.5 vs. 1.6 ± 1.0 , $p < 0.001$ and 3.3 ± 1.9 vs. 2.7 ± 1.4 , $p < 0.001$).

In conclusion, overlapping stroke-AHRE association can be explained on the basis of atrial cardiomyopathy, which has common risk factors. Absence of a distinct temporal association between device-detected atrial arrhythmias and the occurrence of stroke warrants studies investigating this cause or effect relationship.

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Received 2 March 2019
Available online 3 May 2019

<https://doi.org/10.1016/j.jjcc.2019.03.020>

Atrial high-rate episodes and atrial cardiomyopathy on the future stroke



We thank Özcan et al. for their interest in our paper published in the *Journal of Cardiology* [1]. We would like to respond to their valuable comments.

Özcan et al. emphasized that the temporal relationship between device-detected atrial high-rate episodes (AHREs) and the occurrence of stroke was not clear. We demonstrated that atrial fibrillation (AF) episodes detected by cardiac implantable electronic devices (CIEDs) were associated with embolic stroke events in patients who had no prior history of AF and anticoagulant therapy, and that 30 s was the best cut-off time for AHREs for predicting the risk of embolic stroke events in this population [1]. As Özcan et al. mentioned, the time series of AHREs assessed by CIEDs and the onset of embolic stroke events was not evaluated in our study. This is a limitation of our study. However, we believe that AHREs are only one of the markers and may never result in embolic stroke events directly.

In a previous study involving 3464 patients with ischemic stroke, most patients had sinus rhythm on their baseline electrocardiogram (ECG) [2]. As we mentioned in our paper, in a previous study involving 187 patients with acute ischemic stroke, AHREs for 5.5 h within 30 days before stroke events were recorded in only 15% of patients [3]. These findings suggest that AHREs reflect an indirect mechanism related to multiple comorbidities

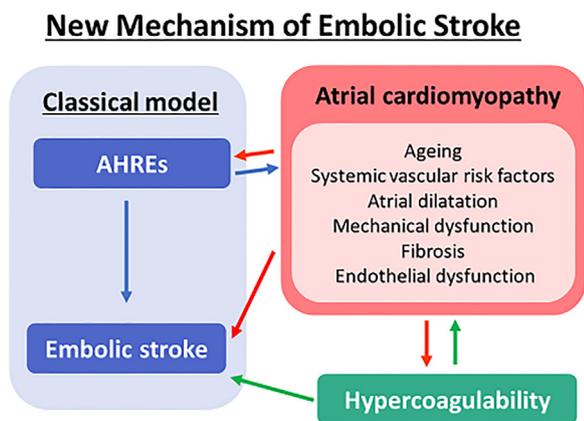


Fig. 1. New mechanism of embolic stroke. AHREs, atrial high-rate episodes.

associated with embolic stroke. Kamel et al. proposed an updated model for thrombo-embolic stroke. They claimed that atrial cardiomyopathy plays a key role and can result in both AHREs and in embolic stroke events, explaining situations in which embolic stroke events precede the occurrence of AHREs. Ageing and systemic vascular risk factors can cause an abnormal atrial substrate leading to atrial cardiomyopathy, which can be characterized by atrial dilatation, mechanical dysfunction, fibrosis, and/or endothelial dysfunction [4]. Fig. 1 summarizes our hypothesis of the new mechanism of embolic stroke events. As a classic model, AHREs directly lead to embolic stroke events. In addition, atrial cardiomyopathy interacted with hypercoagulability, and AHREs could also lead to embolic stroke events. Once AHREs develop, the dysrhythmia causes contractile dysfunction and stasis, which further increases the risk of thromboembolism. Furthermore, this mechanism also has implications for stroke prevention in patients without AHREs. If AHREs serve as a marker of thrombogenic atrial substrates, the benefit seen with anticoagulant drugs in AHREs may extend to patients with atrial cardiomyopathy but no AHREs.

Our data suggested that AF episode lasting for ≥ 30 s might cause atrial cardiomyopathy and could become the risk marker of embolic stroke events. Previous studies revealed that 49–83% of patients with a stroke did not show any AHREs [3–5]. These stroke events might be one of the following outcomes of other pathophysiological mechanisms, i.e. cardiac embolism not related to AHREs, lacunar infarction, arterial dissection and atherosclerosis, or early-phase atrial cardiomyopathy with no manifestation of AHREs. Therefore, it might be difficult to reveal the temporal association between AHREs detected by CIEDs and the occurrence of stroke.

Finally, clarification of the relationship between AHREs and embolic stroke events in patients with CIEDs and the thresholds of AHREs duration that lead to an elevated stroke risk is challenging. It is important that when we detect AF episodes lasting for ≥ 30 s in a patient with CIEDs, we should consider the patient's background and positively consider the prescription of the anticoagulant.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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Received 27 March 2019

Available online 28 June 2019

<https://doi.org/10.1016/j.jjcc.2019.04.012>