Heart rate variability changes following catheter ablation for atrial fibrillation

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Atrial fibrillation (AF) is the most prevalent arrhythmia, which affected 8.8 million adults in Europe in 2010, and this number is projected to grow to 17.9 million by 2060.[1] Patients with AF are at higher risk of developing severe complications such as stroke and heart failure; therefore, AF poses a substantial and growing burden on healthcare systems.[2,3] In the United Kingdom, direct AF-related costs alone in 2000 were 1% of the total National Health Service budget.[4]

The natural history of AF typically shows a progression from paroxysmal to permanent types, and arrhythmia recurs despite optimal rhythm control strategy, including the state-of-the-art interventions such as circumferential pulmonary vein isolation (CPVI) accomplished with catheter ablation.[5] For this reason, it is important to recognize the basic mechanisms involved in the disease process and the way it is affected by treatments in order to develop better treatments or at least identify patients who are more likely to benefit from particular interventions.

The role of altered autonomic nervous system in the pathogenesis of AF has been long recognized.[6] Sympathetic activation promotes arrhythmia by increasing calcium transient in the synapses. In contrast, proarrhythmic effects of parasympathetic activation are mediated by shortening the action potential and refractory period. The autonomic nervous system of the heart is composed of ganglion cells located outside (extrinsic system) or inside the heart (intrinsic system).[6] Both extrinsic and intrinsic nervous systems are important for cardiac function and arrhythmogenesis. The extrinsic system includes parasympathetic fibers from the vagus and sympathetic fibers originating in several cervical and thoracic ganglia. The intrinsic system is mostly found in the atria, formed by colocated cholinergic and adrenergic fibers, and focused at the ganglionated plexi (GP) close to the pulmonary vein (PV) ostia. Data from the experimental models of AF showed that hyperactivity at the GP promotes PV focal activity triggering AF.[7] Increasing evidence shows that GP can also be inadvertently ablated following CPVI.[8] Indeed, in a recent randomized controlled trial in patients with paroxysmal AF, freedom from late AF recurrence was significantly higher in those who received targeted GP ablation with PV isolation as compared with either GP ablation alone or PV isolation alone.[9]

The efficacy of this approach was further assessed in a recent meta-analysis by Kampaktsis et al,[10] where freedom from late AF recurrence was analyzed across 4 randomized controlled trials. The follow-up across the included trials ranged from a minimum of 1 year to 3 years. This meta-analysis showed that AF-free survival in patients with paroxysmal AF was higher following a combination of catheter-based PV isolation and GP ablation. However, in patients with persistent AF, the combination approach showed only a nonsignificant trend toward better outcomes. Thus, the long-term clinical efficacy and safety of GP ablation are not proven. Furthermore, it is important to evaluate which parameters of the cardiac autonomic nervous function are modulated after ablation and whether their assessment can be implemented in routine clinical practice to predict outcomes of CPVI ablation.

Heart rate variability (HRV) is a useful marker of cardiac autonomic nervous system control and has been shown to independently predict all-cause mortality in patients with chronic

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heart failure[11] and those after myocardial infarction.[12] Time and frequency domain methods are the 2 main approaches usually used to assess HRV. From time domain methods, several statistical parameters can be calculated, and one of them is the standard deviation of normal-to-normal intervals. It is calculated as the square root of the variance in successive normal-to-normal R-R intervals and equivalent to total power obtained from the frequency domain methods. This parameter is influenced by the recording time. Calculated for 24 hours, it is considered a gold standard for risk stratification and provides information on overall HRV.[13] The frequency domain indexes of HRV are influenced by respiration and inform about the distribution of power (statistical variance) across the range of frequencies. The ratio of low-frequency (0.04–0.15 Hz) to high-frequency (0.15–0.4 Hz) ranges is considered to be an index of sympathovagal balance, with higher numbers indicating increased sympathetic and / or decreased parasympathetic activity. In patients with sinus rhythm, changes in HRV have been studied very extensively, while scarce data are available on alterations of HRV in patients with AF.

In this issue of *Kardiologia Polska* (*Kardiol Pol*, *Polish Heart Journal*), Marinković et al[14] present the results of their elegant study assessing the relationship between a change in HRV and late AF recurrence in 100 patients following CPVI for paroxysmal AF. They found that HRV was significantly attenuated at 1 day after CPVI in all patients compared with the pre-CPVI values. Furthermore, all HRV parameters remained significantly attenuated for 12 months after CPVI in patients free of late AF recurrence. In contrast, parameters of HRV returned to the preablation level in those who experienced late AF recurrence. Cumulative AF-free survival was significantly higher in patients with the change of the standard deviation of normal-to-normal intervals above 25 ms. The study conclusion was based on the time domain parameters, which are not affected by respiration. This is relevant, as the frequency-domain HRV parameters need to be accounted for respiration characteristics, which are difficult to obtain in routine clinical settings. It is a lot easier to implement 24-hour HRV calculations into routine clinical practice, as Holter monitoring is widely used.

Alterations in cardiac autonomic nervous system function are a critical factor for the initiation and maintenance of AF, and modulating autonomic system balance may contribute to better AF management and more targeted selection of patients potentially eligible for catheter ablation. Future studies are needed to assess the long-term safety of GP ablation and clinical practicalities of routine HRV assessment. Indeed, it would be beneficial to know if GP ablation and subsequent AF-free survival affect left atrial structural remodeling and, ultimately, clinical outcomes.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author are not necessarily those of the journal editors, Polish Cardiac Society, or publisher.

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