Pulmonary vein remodeling in hypertension: Mechanistic insight into primary prevention of atrial fibrillation

To the Editor,

Epidemiological studies have shown that several risk factors, such as increasing age, hypertension, heart failure, myocardial infarction, and valvular heart disease, are known to be independent predictors of the development of atrial fibrillation (AF) (1). Among them, the relative risks due to hypertension are lower, compared with heart failure and valvular disease; however, the population at risk of AF as a result of hypertension is high because it is epidemiologically the most prevalent, especially among the elderly. Therefore, it is important to prevent the development of AF in patients with hypertension. Electrical and structural remodeling in both the atria and the pulmonary veins (PVs) has been observed at the time AF occurred in patients with hypertension (2). Unfortunately, the therapeutic options for structural remodeling (i.e., reverse remodeling) of the atria are currently limited.

Several animal models of hypertension have revealed that left atrial (LA) dilatation and increased interstitial fibrosis led to slowing of conduction and the promotion of AF (3-5). The majority of these animal models were focused on the remodeling of the atria; limited data are available regarding the PVs.

In this issue of the Anatolian Journal of Cardiology, the article "Electrical and histological remodeling of the pulmonary vein in hypertensive rats: indication of initiation and maintenance of atrial fibrillation" investigated the role of electrophysiological and structural PV remodeling in the mechanistic link between hypertension and AF. The authors found that interstitial fibrosis of the LA and PV was greater in two-kidney-one-clip (2K1C) hypertensive rats than in sham rats. In addition, interstitial fibrosis was more prominent in the PVs (27.55±2.20%) compared with the LA (16.96±3.57%), which was consistent with previous reports using a Dahl salt-sensitive hypertension rat model (4). The PVs may be more vulnerable to a pro-fibrotic response due to hypertension than the LA. It is crucial to prevent the progression of fibrotic changes in the PVs. However, it has been reported that treatment for hypertension did not completely eliminate the development of AF associated with hypertension (6). In addition to blood pressure control for hypertension, anti-fibrotic therapy for the PVs, especially in the early stage of hypertension, might be a promising approach for primary prevention of AF in patients with hypertension. The authors also investigated electrical remodeling of the PVs in hypertensive rats, but electrophysiological changes in the PVs in hypertensive rats needs further clarification. This electrophysiological study using conventional microelectrodes was performed only in the LA. The results of protein expression of cardiac ion channels are not always consistent with the electrophysiological results. Further study will be needed to clarify the detailed mechanisms of PV arrhythmogenic substrate for AF due to hypertension. We might need to treat the AF substrate prior to AF onset.

Yu-ki Iwasaki
Department of Cardiovascular Medicine, Nippon Medical School; Tokyo-*Japan*

References

1. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. JAMA 1994; 271: 840-4.
2. Staerk L, Sherer JA, Ko D, Benjamin EJ, Helm RH. Atrial Fibrillation: Epidemiology, Pathophysiology, and Clinical Outcomes. Circ Res 2017; 120: 1501-17. [CrossRef]
3. Choisy SC, Arberry LA, Hancox JC, James AF. Increased susceptibility to atrial tachyarrhythmia in spontaneously hypertensive rat hearts. Hypertension 2007; 49: 498-505. [CrossRef]
4. Iwasaki YK, Yamashita T, Sekiguchi A, Hayami N, Shimizu W. Importance of Pulmonary Vein Preferential Fibrosis for Atrial Fibrillation Promotion in Hypertensive Rat Hearts. Can J Cardiol 2016; 32: 767-76. [CrossRef]
5. Lau DH, Shipp NJ, Kelly DJ, Thanigaimani S, Neo M, Kuklik P, et al. Atrial arrhythmia in ageing spontaneously hypertensive rats: unraveling the substrate in hypertension and ageing. PloS One 2013; 8: e72416. [CrossRef]
6. Schnabel RB, Yin X, Gona P, Larson MG, Beiser AS, McManus DD, et al. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: a cohort study. Lancet 2015; 386: 154-62. [CrossRef]

Address for correspondence: Yu-ki Iwasaki, MD, Department of Cardiovascular Medicine, Nippon Medical School; Tokyo-*Japan*
E-mail: iwasaki@nms.ac.jp
Accepted Date: 30.12.2017

DOI:10.14744/AnatolJCardiol.2017.25931