Editorial

Current Understanding on Mechanisms Leading to Atrial Fibrillation

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► See the article "Association between Serum Parathyroid Hormone Levels and the Prevalence of Atrial Fibrillation: the Dong-gu Study" in volume 48 on page 159.

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Atrial fibrillation (AF) is a rapidly growing disease. Since AF usually occurs in late decades of life, the increase in prevalence in an aging society is an expected phenomenon. Furthermore, as the awareness of disease has increased, more patients are diagnosed and treated for AF every year. According a recently published Korean data, the prevalence and incidence of AF in Koreans is increasing throughout the ages.¹⁾ Increased prevalence of AF also increases socioeconomic burden. Patients with AF are exposed to more than 5 times the risk of stroke, compared to the general population, and the need for stroke prevention continues to rise with the increased prevalence.

Understanding the pathogenesis of AF is an important process in reducing the incidence of disease and in providing appropriate treatment. However, our understanding of the pathogenesis of AF is still lacking. Various mechanisms from various predisposing pathologic causes have been proposed. It is known that the atria are remodeled structurally and functionally due to pathologic causes, and these deformations are an important factor in the development of AF.²⁾ Structural changes of the atria such as stretch-induced atrial fibrosis, hypocontractility, fatty infiltration, inflammation, vascular remodeling, ischaemia, and functional changes such as ion channel dysfunction, and calcium instability occur in the remodeled atria.²⁾

Electrophysiologic changes also play an important role in the development of AF. Structural and functional changes as described above can affect the refractory period of the atrial tissue and increase the incidence of atrial ectopic beats.³⁾ Also, various cardiovascular diseases that influence the autonomic tone may also influence the occurrence of AF. It is understood that triggered activity and changes in substrate due to such electrical changes affect the occurrence and maintenance of AF.⁴⁾

Genetic predisposition also cannot be ignored.²⁾ A considerable portion of AF occurring in younger ages is known to be associated with a genetic predisposition than the accompanying disease. Some studies have reported that more than 30% of atrial fibrillations have a common genetic variation. Among the various known genetic factors, the most important variants are located close to the paired-like homeodomain transcription factor 2 gene on chromosome 4q25.⁵⁾ This genetic variation is known to be associated with up to a 7-fold increase the incidence of AF. In addition to the genetic variants that are likely to cause AF itself, gene mutations that contribute to the atrial remodeling process and electrophysiological changes described above may also mediate the occurrence of AF.

In order to better understand and reinforce new knowledge about AF mechanism, it is important to understand what disease or condition can be a predisposing factor for AF. Various designs of research can be constructed for this purpose. First, we can compare the incidence of AF in a case-cohort study by long-term observation in a large community based cohort. However, due to the various factors affecting the outcome, it is difficult to control all the confounding factors associated with AF. Besides, due to the high proportion of asymptomatic patients, it is difficult to detect new AF. Another way to understand the pathophysiology is to find how AF patients differ from the general population through cross-sectional studies. However, a major limitation of cross sectional studies is that the causal relationship of AF and studied factor are not definite. Nevertheless, it can be said that understanding the characteristics of patients with AF that differ from the general population can improve the understanding of disease and offer insights that can lead to future studies.

There have been many previous reports on the clinical features of AF patients. In the Framingham Heart Study cohort, various cardiovascular risk factors have been shown to be causative factors of AF,⁶⁾ and C-reactive protein, a biomarker representing inflammation, has also been reported to have a significant association with AF.⁷⁾ In Korea, Big Data has reported that proteinuria is a risk factor for AF,⁸⁾ and it has been reported that the prognosis is poor when the red blood cell distribution width (RDW) level is elevated.⁹⁾

In this context, the article “Association between Serum Parathyroid Hormone Levels and the Prevalence of Atrial Fibrillation: the Dong-gu Study” discusses increased parathyroid hormone (PTH) levels as a peculiarity of AF patients.¹⁰⁾ The authors state how PTH levels associated with calcium homeostasis can contribute to the development of AF, while AF itself raises the PTH level at the same time. The authors also report a higher serum PTH level is associated with a higher prevalence of AF, in a well-sorted large Korean adult cohort of 9,007 patients. Because calcium instability constitutes an important part in the mechanism of occurrence of AF, the authors' suggestion of targeting PTH in a large-scale analysis has clinical implications. If follow-up data is accumulated in the future, more patient-focused results could be obtained.

In summary, despite the high prevalence and numerous studies, we still do not fully understand the mechanism of AF development. The authors' work on AF and PTH will play a role as a basis for future research. We expect to see additional research on this subject, including follow-up data of the cohort, in the near future, and the authors deserve to be congratulated on their excellent idea and work.

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