AF certainly induces remodeling in some areas other than the LA, and these include pulmonary veins (PV) and ganglionated plexi (GP) existing in the epicardial fat pad. Reportedly, patients with AF usually have larger PV than control subjects, but those with paroxysmal AF do not have larger LA than controls, suggesting that AF per se may result in anatomic PV remodeling. Because the PV-LA junction has no anatomic valves, LA contraction allows PV regurgitation to a small extent. Myocardial sleeves extending from LA surround the proximal PV and act as a sphincter to minimize PV regurgitation. Myocardial sleeves in AF patients are arrhythmogenic, showing slow conduction, low voltage, and inhomogeneous refractoriness. Furthermore, PV regurgitation presumably causes highly compliant PV dilatation, myocardial sleeve stretching, and repetitive focal firing, which triggers AF. This arrhythmogenic activity may suppress rhythmic PV contraction, which allows further PV regurgitation and dilatation, forming a vicious cycle. A study using multi-detector computed tomography (MDCT) demonstrated the poor contractility of bilateral superior PV in patients with paroxysmal AF. Moreover, radiofrequency (RF) catheter ablation to achieve PV isolation has been reported to reduce the LA volume and PV size, and restore PV contractility. This line of evidence indicates that RF ablation has the potential to reverse contractile and structural PV remodeling.

GP is also responsible for AF pathophysiology, and is a target of RF ablation. Cardiac autonomic tonus is elevated by a brief period of AF in an accentuated sympathovagal antagonistic manner. In a canine AF model, autonomic neural remodeling is evident in the posterior LA and PV, contributing to the positive feedback mechanism that explains “AF begets AF.”

Sympathetic hyperinnervation facilitates triggered activity under the intracellular Ca\(^{2+}\) overload, whereas vagal hyperinnervation shortens atrial effective refractoriness inhomogeneously, allowing multiple unstable reentrant circuit formation. In a clinical MDCT study, the GP-containing epicardial fat pad mass is greater in AF patients than in controls, and is an independent predictor of post-ablative AF recurrence. These investigations indicate that AF induces functional and anatomic autonomic neural remodeling.

In contrast, there has been little attention paid to AF-induced structural remodeling in the right atrium (RA). The coexistence of AF and isthmus-dependent common atrial flutter (AFl) is well known. AF precedes the onset of AFl, and AF recurrence is recognized after concurrent isthmus ablation and PV isolation in many of such cases. Because the RA size and isthmus length are determinants of common AFl, these imply that AF-induced remodeling expands to the RA, and that non-PV foci in RA underlie AF recurrence. In this issue of the Journal, Moon et al investigated the relationship between RA anatomical remodeling and the outcomes of non-valvular AF treated with RF ablation. Consequently, the RA volume index assessed on MDCT alone was an independent predictor of early, but not late (ie, 1-year), recurrence of AF after successful RF ablation. A cardiac MDCT study published immediately prior to this article and which analyzed both atrial remodeling and AF recurrence, also agreed with the Moon et al findings. These studies, however, cannot necessarily be generalized to all AF patients. The Moon et al study was performed on the basis of RF ablation. Therefore, patients with AF showing advanced LA remodeling were not enrolled. In their study group of AF patients, the RA volume index was significantly proportional to the LA volume index, and the extent of atrial anatomical remodeling correlated with AF chronicity, indicating simultaneous anatomical remodeling of both atria according to the progression of AF.

One important question remains in the Moon et al study concerning the role of RA anatomical remodeling in the early recurrence of non-valvular AF. Incomplete oval fossa closure (25–30% of the general population) and the existence of interatrial muscle connections may allow ‘transmission’ of atrial fibrillation (AF) to the RA, which appears to be susceptible to the positive feedback mechanism. This phenomenon may explain why AF recurrence after RF ablation is greater in the RA than the LA. Consequently, the RA may be an actual target of RF ablation, and investigation of RA remodeling may provide evidence about the significance of RA remodeling to AF recurrence. The evidence of RA remodeling, however, should be associated with the direct visualization of RA remodeling observed in areas other than the LA has drawn little attention so far.

Atrial fibrillation (AF) is one of the most common arrhythmias observed in clinical practice. It is well known that paroxysms of AF become longer, that AF becomes refractory to pharmacological rhythm-control treatment, and that the electrical defibrillation threshold is gradually elevated. The most accepted concept explaining these clinical phenomena is so-called remodeling. There is a body of evidence with respect to the time course of AF-induced remodeling: that is, that electrical remodeling affecting the expression and function of various cardiac ion channels occurs at first, then, contractile remodeling follows, and, finally, structural remodeling takes place leading to left atrial (LA) mechanical dysfunction and enlargement. LA is undoubtedly the most accepted site of remodeling caused by AF, whereas remodeling observed in areas other than the LA has drawn little attention so far.
remodeling. Complex fractionated atrial electrograms, considered as a nest of AF, are observed in both atria including the crista terminalis, septum, superior vena cava, and coronary sinus ostium in patients with persistent AF, suggesting both atrial fibrosis under the advanced remodeling and the necessity of arrhythmogenic substrate modification of both atria. Among several cardiac imaging modalities, echocardiography has a limited potential for precise RA volume estimation. Müller et al reported reverse RA anatomical remodeling after successful PV isolation using 3-D echocardiography. As Moon et al mentioned, a large cohort is warranted to confirm reverse RA anatomical remodeling in patients with ablated AF using more sophisticated imaging techniques.

References