trial fibrillation (AF) is one of the most common forms of cardiac arrhythmias encountered in clinical practice, and is associated with serious clinical consequences such as systemic thromboembolism, heart failure, and increased mortality. AF is a highly age-related condition, so with the progressive aging of the Japanese population, the number of individuals with AF is expected to increase in the coming decades. There is convincing evidence of a pathophysiological association between AF and left atrial (LA) remodeling. LA remodeling includes structural, functional, electrical, metabolic, and neurohumoral changes that occur in response to several pathologic processes. However, the underlying mechanisms of LA remodeling in AF are not fully elucidated (Figure). For instance, AF may cause LA dilatation, a hallmark of LA structural remodeling, which may in turn promote AF. The causal relationship between AF and LA structural remodeling is therefore rather complicated. Histologically, LA structural remodeling is characterized by atrial fibrosis, the excessive deposition of extracellular matrix protein produced by fibroblasts. Atrial fibrosis is thought to contribute to the pathogenesis of AF via multiple mechanisms, including increased chamber stiffness, impaired electrical activity of myocytes through abnormal myocyte-fibroblast coupling, and conduction abnormalities induced by fibrotic tissues. Structural remodeling may

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therefore play a causal role in the development of functional or electrical LA remodeling in AF, although it is also reported that LA functional remodeling precedes structural remodeling in paroxysmal AF patients.

Structural LA remodeling has prognostic implications. LA size is a strong predictor of subsequent cardiovascular events in patients with lone AF, independent of age and clinical risk factors. Increased LA size is also a predictor of subsequent AF development in the general population. Furthermore, increasing evidence shows that LA remodeling is reversible after therapeutic interventions. For instance, restoration of sinus rhythm from AF, whether by electrical cardioversion or radiofrequency ablation, results in reversal of LA enlargement. Although the direct effect of LA reverse remodeling on cardiovascular outcomes remains to be seen, the evidence suggests that a decrease in LA size is associated with reduced risk of AF recurrence.

Recent advances in both catheter ablation technology and our understanding of the pathophysiology of AF have made radiofrequency catheter ablation a potentially curative therapeutic strategy for AF. Indeed, the number of AF patients treated with catheter ablation is constantly increasing. However, catheter ablation is not necessarily effective for all patients and the relatively high recurrence rate is also a major challenge. In this regard, preprocedural screening of AF patients who are suitable for catheter ablation is critical for optimizing the success and safety of the procedure, and identification of clinical factors that predict the maintenance of sinus rhythm after catheter ablation is of clinical relevance to reduce healthcare costs and avoid exposing patients to unnecessary procedures and related complications.

In this issue of the Journal, the study by Machino-Ohtsuka and colleagues shows that LA reverse remodeling after catheter ablation is associated with better LA/LAA appendage (LAA) function, both at baseline and at 12 months after ablation, and that parameters of LA/LAA function can predict the outcome of catheter ablation (maintenance of sinus rhythm and LA reverse remodeling) in patients with persistent AF. The study consisted of 123 patients with symptomatic drug-refractory persistent AF who underwent radiofrequency catheter ablation. During a mean follow-up of 18 months after catheter ablation, AF reverted to sinus rhythm without subsequent recurrence in 78 patients (63%), and 62 of these patients had accompanying reverse remodeling of the LA (≥15% reduction in LA volume at follow-up). In multivariable models, the echocardiographic indices of greater global LA systolic strain and greater LAA wall velocity were independent predictors of LA reverse remodeling, as well as maintenance of sinus rhythm. The study also showed that reversal of LA structural remodeling was associated with further improvement of LA/LAA function at follow-up.

The advantages of echocardiographic assessment are clear: simplicity of data acquisition, less invasiveness, absence of radiation exposure, cost-effectiveness, portability, and adaptability. The few contraindications to either transthoracic or transesophageal echocardiography ensure greater accessibility. Moreover, recent advances in the imaging technology enable precise assessment of LA/LAA function even in patients with AF. For instance, LA strain and strain rate can be measured by transthoracic echocardiography with the use of 2-dimensional speckle tracking echocardiography. Previous studies have demonstrated that these newer parameters are reproducible and more sensitive than conventional measurements in identifying early changes in LA function. Although there has been concern that clinical assessment of cardiac function during AF may be difficult because of beat-to-beat variation in myocardial contractility, it is now established that hemodynamic parameters can be accurately estimated in patients with AF using the index beat (ie, the beat following 2 preceding cardiac cycles of equal duration). Therefore, LA strain and strain rate obtained from the index beat can be used as sensitive indices of LA function in patients with AF.

Transesophageal echocardiography provides essential information about the LAA, which is a highly contractile structure with a pattern of contractions totally different from that of the LA main body. It is more compliant and therefore plays an important role in the LA reservoir function, especially when the LA pressure or volume is increased. The LAA is the source of more than 90% of non-valvular AF-related thrombi, causing stroke, infarction, and emboli. Reduced LAA function results in impaired blood exchange with the LA main body, which is thought to be the mechanism of thrombus formation in the LAA. LAA flow velocity and wall motion velocity measured by transesophageal echocardiography reflect active contraction of the LAA and are useful indices of LAA function.

The report by Machino-Ohtsuka and colleagues demonstrates that combined evaluation of the LA and LAA function improves prognostication after catheter ablation in patients with persistent AF. This notion is supported by another recent report in which global LA strain at late diastole was shown to be a predictor of early AF recurrence after catheter ablation. It should be noted that LA volume was not a statistically significant predictor of AF recurrence after catheter ablation in either study, suggesting that functional LA remodeling may be more sensitive than structural LA remodeling in predicting the outcome of AF ablation.

In conclusion, comprehensive evaluation of LA/LAA function may both refine risk stratification and guide therapy in patients with AF. Whether LA reverse remodeling after successful catheter ablation reduces the burden of adverse clinical consequences is an important clinical question that remains to be elucidated by future studies.

Disclosures
There are no conflicts of interest on the part of the author.

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