Obesity is a major risk factor for cardiovascular disease, including atrial fibrillation (AF). However, the mechanisms for this association have not been well clarified. Recent studies suggest that obesity-related diseases may be mediated, at least in part, by regional adipose deposits. For example, expansion and inflammation of perivascular adipose tissue have been implicated not only in the development of endothelial dysfunction and atherosclerosis, but also in the pathogenesis of insulin resistance. Furthermore, several studies have shown that epicardial adipose tissue (EAT) is not only an anatomic depot of fat, but also may serve as a local source of proinflammatory cytokines related to coronary artery disease (CAD). Although there are several studies reporting an association between EAT and CAD, the evidence concerning the association between EAT and arrhythmia is relatively limited.

A recent report showed that EAT volume measured by computed tomography (CT) was highly associated with AF, independent of traditional risk factors including left atrial (LA) enlargement. Another study using a relatively large sample from the Framingham Heart Study (n=3,217) has also shown that pericardial fat volume was associated with AF even after adjustment for risk factors, including body mass index. In addition, Wong et al recently reported that EAT volume assessed by magnetic resonance imaging (MRI) was significantly associated with AF chronicity and symptom burden, as well as the presence itself, and is predictive of long-term AF recurrence after ablation. These results suggested that EAT may play a role in the pathogenesis of AF. However, those studies did not specify the amount and distribution of EAT surrounding the atrium.

In this issue of the Journal, Nakanishi and colleagues investigate the relationship between peri-atrial EAT volume measured by multidetector CT and new-onset nonvalvular AF in 279 patients with no history of AF. They demonstrate a close association between peri-atrial EAT volume and the development of new-onset AF; independent of the presence of hypertension, diabetes, or LA enlargement, although a recent study demonstrated that, among several types of epicardial fat, only peri-atrial epicardial fat thickness at the esophagus was associated with AF burden independent of age, body mass index, or LA area. Nakanishi et al have demonstrated for the first time that peri-atrial EAT volume predicted future AF events more accurately than total EAT volume during follow-up of 3.3±1.0 years. These results suggest the potential role of peri-atrial EAT in the development of AF. Peri-atrial EAT, because of its contiguity with atrial tissue, may have local and direct effects on LA structures, generation of inflammatory cytokines, and modulation of the intrinsic autonomic nervous system. Because EAT is postulated to be a source of inflammatory mediators, peri-atrial EAT may promote the activation of ectopic foci in the pulmonary vein ostia or create the atrial substrate for AF via several inflammatory mediators, including adipocytokines. Further studies are needed to determine whether peri-atrial EAT causes inflammation and subsequent AF or is merely associated with inflammation and AF.

If peri-atrial EAT contributes to the development of AF, how might this occur? One possible mechanism is that paracrine release of inflammatory mediators from peri-atrial EAT could traverse the atrial wall by diffusion from “outside-to-inside” or via small channels to interact with atrial cells. On the other hand, Yamashita et al showed that the distribution of immune cells was heterogeneous and atrial endomyocardium and subendomyocardium were more subject to infiltration by immune cells than the midmyocardium in AF patients. They suggested recruitment of immune cells across the atrial endocardium as a possible mechanism for inflammation in AF. These opposing mechanisms underlying AF are similar to those in atherosclerosis. Although the current concept is that inflammatory signaling originating from the endothelium plays a key role in the development of atherosclerotic lesions, there is growing evidence that changes in the adventitia or perivascular adipose tissues could also alter vascular homeostasis. The mechanisms whereby epicardial adipocytokines may potentially play a role in coronary atherosclerosis include paracrine and vasoactive signaling via the vasa vasorum. It is plausible that peri-atrial EAT may modify the development of AF by secreting inflammatory cytokines into the atrial wall and possibly the pulmonary vein ostia (Figure).

There are potential clinical implications of the association between EAT and AF. Several recent studies, including this study by Nakanishi and colleagues, have established the association of EAT with AF as independent of other risk factors and systemic adiposity. The volume of EAT, especially peri-atrial EAT, measured by CT or MRI might yield additional information on the risk for AF onset, progression, and recurrence after ablation therapy.

However, the therapeutic implications of the association between EAT and AF remain unknown. Weight loss has been...
shown to lead to marked reductions in pericardial fat and may limit the potentially adverse effects of pericardial fat deposits, including changes in cardiac morphology and function. The effects of some pharmacological therapy on EAT have been evaluated. A recent study showed that treatment with pioglitazone in type 2 diabetic patients with CAD was associated with a reduction in inflammation-related gene expression in EAT. Moreover, another study reported that patients treated with atorvastatin showed more significant reductions in epicardial fat thickness as measured by echocardiography than patients treated with simvastatin/ezetimibe. Strategies to reduce peri-atrial EAT volume might be effective in decreasing the incidence and recurrence of AF. Further studies examining the effects of weight loss or pharmacological interventions on peri-atrial EAT volume and AF prevalence are needed.

References