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Commentary

Adipocytokines modulate ionic currents – A key to lipotoxicity potentiated cardiac arrhythmia

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Obesity with excessive fat was an important risk factor for the occurrence or progression of cardiac arrhythmia. As compared to abdominal fat, the amount of epicardial fat more correlates with the occurrences of atrial fibrillation, which suggests the distinctive arrhythmogenic effects of epicardial fat. Adipose tissue secrets numerous adipocytokines, thus epicardial fat may have more cardiac effects than other body fat [1]. Adipocytokines can enhance local inflammation and generate myocardial remodeling, which play a role in the pathophysiology of arrhythmia. Fatty infiltration or fatty metamorphosis can induce abnormal automaticity from degenerated myocardial cells. Adipose tissues also serve as obstacles for an activation wave front or by producing atrial fibrosis, which may interfere with atrial conduction and enhance the generation of reentry circuits.

Lee et al. investigated the effects of adipocytokines from different body fats on delayed rectifier K^+ outward currents (I_{Kr}) in cardiomyocytes [2]. In their study, H9c2 cells were treated with adipocytokine-free medium (the Adipo-free group), and with adipocytokines from rat epicardial (central fat group) or limb (peripheral fat group) fat tissues. They found that adipocytokines significantly decreased I_{Kr} in H9c2 cells, and I_{Kr} was more prominently decreased by adipocytokines from epicardial fat than from limb fat. Although the mechanisms were not fully elucidated, Lee et al. pointed out the direct electrophysiological effects of adipocytokines and also demonstrated stronger ionic effects of epicardial fat than other body fat. Decreased I_{Kr} can prolong action potential duration and facilitate the arrhythmogenesis due to triggered activity with early after depolarization. Besides, inhomogenesis fatty infiltration can enhance dispersions of action potential duration, which also increases the possibility of reentry circuit genesis.

Our previous experiments also showed that adipocytes directly modulate rabbit cardiomyocytes ionic currents with decreases of I_{Kr} and inward rectifier potassium currents [3]. The epicardial adipocyte-incubated left atrial myocytes had significantly more positive resting membrane potential than control left atrial myocytes. In addition, epicardial adipocytes can increase atrial myocytes late sodium currents, L-type calcium currents, and transient outward potassium currents with a higher incidence of isoproterenol induced triggered beats. However, these in vitro studies were only carried out for a short period in animal experiments, it was not clear whether human fat also have similar effects. In addition, different incubation times may result in variable outcomes.

The associations between the amount of fat tissue and an increasing incidence of cardiac arrhythmias had been reported in recent years [4–9], even though that removing epicardial fat during cardiac surgery did not decrease the occurrence of atrial fibrillation [10]. An interesting case had been reported that ablation of high-dominant frequency sites covered with epicardial adipose tissues can terminate atrial fibrillation [11]. High-dominant frequency sites are known to be related to the center of focal-firing rotors or local reentry circuits. Moreover, high-dominant frequency sites, but not complex fractionated atrial electrogram sites are located adjacent to epicardial adipose tissue sites [12]. Therefore, epicardial adipose tissues were suggested to be involved in the maintenance of atrial fibrillation. Nevertheless, the mechanisms underlying epicardial fat tissues on cardiac arrhythmia remain obscure.

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The responsible adipocytokines and underlying mechanisms for the observed effects were not elucidated in Lee's study. Since mixed adipocytokines could have opposite effects that may have canceled out a measurable effect on myocyte electrophysiology, it is critical to clarify the individual effects of different adipocytokines. Additionally, epicardial fat from failed hearts has more fat-induced atrial arrhythmia than fat from healthy hearts [13]. Therefore cardiovascular diseases may change the arrhythmogenesis and adipocytokines in epicardial fat. Future studies are mandatory to answer the questions inspired from Lee's study. In addition, to find the adipocytokine underlying the distinctive electrophysiological effects of epicardial fats may lead into a new treatment strategy for obesity related cardiac arrhythmia.

Conflict of interest

There is no conflict of interest related to this article.

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