New trials for assessment of left atrial dysfunction by FDG-PET

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The left atrium (LA) has an important role in modulating left ventricular filling and maintaining cardiac output.¹ In addition, LA has been identified as an important biomarker of cardiovascular disease and adverse cardiovascular outcomes.^{2,3} Therefore, LA function has been focused for precisely and quantitatively analyzed recently. However, most of functional studies of LA have so far been done by echocardiography.^{4–6}

Atrial fibrillation (AF) leads to progressive structural and functional changes in LA over time. LA fibrosis is a major determinant of the progression to, and burden of AF and its substrate, leading to an increase in total atrial activation time.^{7,8} A fibrosis burden demonstrated on late gadolinium contrast-enhanced cardiac magnetic resonance.^{9,10} There is evidence of progressive remodeling of the LA once AF develops with increasing fibrosis alongside lower LA reservoir strain in patients with persistent AF compared with patients with paroxysmal AF (PAF).⁹

PET has played an important role for functional and molecular imaging of the heart. FDG-PET has been used for identifying focal tumor lesions in atrial areas.¹⁰ With improvement of image quality, PET has recently been used for assessing atrial tissue function.^{11,12} Of particular, FDG-PET has been used for assessing AF. With maximal use of high-resolution PET, it has a potential

for identifying focus of AF as well as for assessing left atrial function quantitatively.

FDG is a glucose analog and has been used for tracking glucose metabolism. FDG-PET has two completely different roles for cardiovascular imaging. FDG-PET has long been used for assessing tissue viability for patients with coronary artery disease.¹³ The heart derives its energy mainly from free fatty acids and glucose. FDG commonly enters cardiomyocytes through the glucose transporters 1 and 4. In ischemic state with the availability of glucose, FDG accumulation in the myocardium is maintained due to the dominant anaerobic glucose metabolism. On the other hand, FDG-PET has recently been used for identifying active inflammatory lesions because glucose is also consumed in the inflammatory process.^{14,15}

Depending on the purposes of in vivo functional imaging, patient preparation should be carefully done before the FDG administration.^{16–18} Post-prandial condition, glucose loading, or insulin clamp is applied for myocardial viability assessment, whereas long fasting condition with or without heparin administration is required for identifying active inflammatory lesions with suppressing physiological myocardial FDG uptake.

The current paper includes retrospective clinical study to understand the feasibility of FDG-PET/CT under insulin clamp condition in order to relate scar and metabolic parameters identified by this method with structural and electrical remodeling across patients with varying degrees of AF burden in patients with sinus rhythm, PAF, and persistent AF.¹⁹ Ghannam and colleagues suggested that greater AF burden correlates with increased LA metabolism and scar. They have correlated the newly obtained metabolic activity with various structural parameters as well as ECG functional parameters. They suggested that those with AF may have greater LA volumes, increases in the amount and heterogeneity of LA metabolism, and greater amount of LA scar.

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It would be interesting to see potential mechanism to increase in FDG uptake in LA. If the increased metabolism of LA is secondary to AF in patients with HFrEF, what is the mechanism? Is hypometabolic scar a primary change to induce AF or a secondary change due to LA remodeling? Was this phenomenon due to partial volume effect as a result of increase in LA thickness or actual increase in glucose metabolism due to AF? The authors used both FDG and perfusion PET studies. What were the differences in perfusion and metabolism in LA areas in three different groups? It would be valuable to see whether AF may alter metabolism more than perfusion. The authors considered the inter-atrial septum to be part of the LA. But an elevated right atrial pressures may possibly influence FDG uptake in the inter-atrial septum. Thus, hemodynamic parameters may impact atrial metabolism. It would be nice to adjust for hemodynamic parameters during image acquisition.

Furthermore, some technical limitations should be discussed. There are significant partial volume effects for estimating metabolism as well as perfusion in thin wall, such as LA. Wall thickening in LA overload may significantly overestimate LA metabolism in AF as compared to sinus rhythm. In addition, ECG-gated acquisition may be required for precise assessment of tracer uptake in those with sinus vs AF. An image motion artifact may possibly underestimate metabolism and scar in AF as compared to sinus rhythm on gated acquisition. Second, delayed image (scan after 2-4 hours rather than 50 minutes) might improve the contrast between LA wall and LA cavity to detect slight uptake of the thin structure.

In order to validate the current unique and attractive findings, many more patient studies (preferably prospective study) using FDG-PET may be required. In addition, a precise comparison of ECG findings with various LA functional parameters is suggested using multi-imaging modalities, such as echocardiography, MRI, and PET perfusion and metabolic imaging. A high-resolution gadolinium-enhanced MRI (LGE) may hold a promise for precise assessment of LA scar and LA function simultaneously. On the other hand, FDG-PET with Rb-82 perfusion can be done in any patients even after cardiac device installation. Moreover, PET may provide important information such as molecular and biochemical alterations in LA. Although the clinical importance to assess LA metabolism in addition to the size of LA is still unknown, hypometabolic scarring or its heterogeneity might predict patients with AF refractory to antiarrhythmic drugs and ablation therapy. In fact, AF is a significant predictor of heart failure hospitalization in patients with HFpEF.²⁰ Potential mechanisms of LA remodeling and correlation with LA scar and regional dysfunction should fully be

discussed. The current study raises the several interesting questions regarding LA metabolism in AF and heart failure.

Disclosures

The authors declare that there is no potential conflict of interest to disclose.

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