Remodeling of myocardial energy and metabolic homeostasis in a sheep model of persistent atrial fibrillation

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**Introduction**: Atrial fibrillation (AF) is the most common progressive cardiac arrhythmia and is often associated with rapid contraction in both atria and ventricles. The role of atrial energy and metabolic homeostasis in AF progression is under-investigated. To determine the remodeling of energy metabolism during in persistent AF and the effect of eplerenone (EPL), an aldosterone inhibitor, on metabolic homeostasis.

**Methods**: A nonsustained atrial pacing sheep model was developed to simulate the progression of AF from paroxysmal to persistent. Metabolomic and proteomic analyses at termination of the experiment were used to analyze atrial tissues obtained from sheep in sham, sugar pill (SP) and EPL-treated groups.

**Result**: Proteomic analysis indicated that compared to the sham group, in SP group, fatty acid (FA) synthesis, FA oxidation, tricarboxylic acid (TCA) cycle processes and amino acids (AAs) transport and metabolism were reduced, while glycolytic processes were increased. In metabolomics analysis, the levels of intermediate metabolite of the glycolytic pathways, including 2-Phosphoglyceric acid (2PG), 1,3-Bisphosphoglyceric acid (1,3PG), and pyruvate, HBP (uridine diphosphate-N-acetylglucosamine, UDP-GlcNAc), TCA (citrate) and AAs were greater while the levels of the majority of lipid classes, including phosphatidic acid (PA), phosphatidylcholine (PC), phosphatidylglycerol (PG), glycerophosphoglycerophosphates (PGP), glycerophosph glycerophosphoinositols (PI) and glycerophosphoserines (PS), were decreased in the atria of SP group than in those of sham group. EPL-treatment decreased glucose uptake and increased the content of acylcarnitines and lipids, such as lyso phospholipids, phospholipids and neutral lipids.

**Conclusion**: In the metabolic remodeling during AF, glucose and lipid metabolism were up- and down-regulated, respectively, to sustain TCA cycle anaplerosis. EPL partially reversed the metabolic shifting.