Downregulated serum 14, 15-EET is associated with abdominal aortic calcification in patients with primary aldosteronism

With the support by the National Natural Science Foundation of China, the research team directed by Prof. Huang Hui (黄辉) at Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, recently reported that aldosterone is an important promotor of abdominal aortic calcification, which was published in *Hypertension* (2018, 71(4): 592—598).

The prevalence of chronic kidney diseases (CKD) is increasing and the estimated number of adult CKD in China has reached 120 million. Despite the improvement of dialysis techniques, CKD mortality continues to increase and cardiovascular events are still the leading cause of CKD deaths. Notably, previous studies of their group demonstrated that vascular calcification (VC) is an important predictor of cardiovascular events in CKD (*Arterioscler Thromb Vasc Biol*, 2017, 37(10): 1933—1943).

It is well-known that the excessively activated renin-angiotensin-aldosterone system (RAAS) plays an essential role in the progression CKD and cardiovascular events. Increased angiotensin II and aldosterone components are the most important effectors. It was shown that aldosterone excess promoted vascular inflammation and oxidative stress, resulting in vascular remodeling. However, the relationship between aldosterone and VC remains unclear, especially lack of direct evidence from human studies. In addition, both plasma aldosterone concentration and the prevalence of VC are elevated in CKD. Thus, it is difficult to confirm whether it is a parallel or causal relationship. Their research team observed there was no relationship between aldosterone and coronary artery calcification in hypertensive population. Interestingly, in those with an impaired estimated glomerular filtration rate (eGFR), the risk of VC is significantly increased when plasma aldosterone concentration elevates. Compared with essential hypertensive patients matched by age and blood pressure, primary aldosteronism (PA) with impaired eGFR had significantly higher plasma bone metabolism factors, accompanied by almost 1-fold higher abdominal aortic calcification (AAC) prevalence (39.1% vs 20.3%, $P=0.023$). It indicates aldosterone promotes VC only in condition with impaired kidney function. Moreover, their group also found that primary aldosteronism patients with AAC exhibited higher 14, 15-dihydroxyeicosatrienoic acid (14, 15-DHET), the inactive metabolite of 14, 15-epoxyeicosatrienoic acid (14, 15-EET) by sEH from arachidonic acids. The research team has focused on the translational researches about EETs for a long time, and the results of this present study suggested that regulation of 14, 15-EET may be a promising target in kidney and cardiovascular diseases.

These findings demonstrated the positive correlation between aldosterone and VC in human study. In the calcifying micro-environment provided by impaired kidney function, aldosterone may significantly promote progression of VC and 14, 15-EET is a potential target for intervention. Taken together, it provides new insights into the relationship between osteoprosis mineral and VC *via* aldosterone, which may help to find effective treatment strategies of VC.

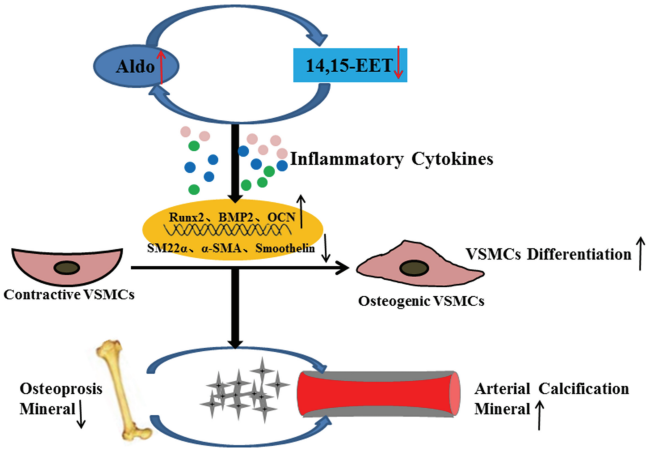

Figure Working model for the mechanism of aldosterone excess and downregulated 14, 15-EET to activate inflammation, which further promotes osteogenic differentiation of vascular smooth muscle cells, resulting in bone loss and increased vascular calcification.