**LEFT ATRIAL APPENDAGE THROMBOSIS IN A MOUSE MODEL OF CORONARY ARTERY DISEASE**

**H.J. Begmatov**, O. Rashidbaigi, F. Romanelli, A.M. Corbo, J. Millan, M. Plummer,

O.V. Savinova

NYIT College of Osteopathic Medicine, Old Westbury, NY, USA

**Objective:**The objective of this study was to examine the frequency of left atrial appendage (LAA) thrombosis in a mouse model of coronary artery disease (CAD) induced by tissue-nonspecific alkaline phosphatase (TNAP) overexpression.

**Background**: Non-valvular atrial fibrillation (NVAF) is most common arrhythmia that is associated with approximately 5-fold increase in the risk for stroke and 2-fold increase in the risk for all-cause mortality. Left atrial appendage thrombosis, which is due to chronic atrial fibrillation, is associated with an estimated 39% cases of CAD (Stoddart, 1995) and patients with NVAF and CAD have poorer prognosis. Although anticoagulant therapy reduces stroke and cardiovascular death, 2.7% of NVAF patients still experience LAA thrombosis despite ongoing anticoagulation (Kawabata, 2017; Da Costa, 2017). Surgical excision is an option for patients who cannot tolerate anticoagulants or in whom anticoagulation is ineffective; this approach however may cause serious perioperative complications. At the present, studies of the pathogenesis of LAA thrombosis in animal models are limited and no reliable model of spontaneous LAA thrombosis exists (Yoshizawa, 2005).

**Methods and Results:** LAA thrombosis was examined in a new model of accelerated CAD in mice (Romanelli, 2017). Two groups of mice, WHC (resistant to CAD) and WHC-eTNAP (susceptible to CAD, due to TNAP-induced arterial calcification), were compared. Histological examination of LAA was performed in serial sections stained with H&E. CAD was confirmed by calcium and lipid-specific staining of coronary arteries. Echocardiographic study showed reduced ejection fraction (EF) in the CAD group compared to the control group. In the WHC group we did not observe LAA thrombosis (n = 23). In the WHC-eTNAP group, however, we observed LAA thrombosis in 8 out of 21 mice. The LAA masses displayed a typical structure of organized thrombi.

**Conclusions:**  In our mouse model, CAD is associated with high prevalence of LAA thrombosis (38%). We suggest that overexpression of TNAP can cause endothelial damage that in the presence of hemostasis (reduced EF) can create LAA thrombosis. This requires further investigation.