Abstract: **P371**

**High Fat Diet-induced obesity induced AF vulnerability, shortened action potential and imbalanced potassium currents in mice atria**

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Background. Obesity is an independent risk factor for atrial fibrillation (AF) the most frequent cardiac arrhythmia in clinical practice. Several mechanisms have been proposed to explain this epidemiological observation including epicardial adipose tissue expansion promoting sub-epicardial fibrosis accumulation, adipokines secretion or free radicals. Moreover, increase in potassium channels expression has been reported in atrial myocardium obese mice.

Purpose. To characterize the atrial electrical properties of obese mice induced by 2 or 4 months of a high fat diet (HFD).

Methods. Eight weeks old C57Bl/6J mice were subjected to 2 or 4 months of HFD (60% fat) or normal diet (ND, 4% fat). Rapid burst atrial pacing were delivered using a trans-esophageal probe to induced AF in anesthetized animals. For action potential (AP) recordings, left atrium (LA) were harvested and maintained at 35°C with continuous 95% O2/5% CO2 gassing. Atrial tissue AP were recorded using glass microelectrode technique. For potassium currents recordings, both atria were harvested and enzymatically digested with a mix of enzymes at 37°C under smooth agitation. ATP-dependent potassium current, IK,ATP, considered as the glibenclamide sensitive current, inward rectifier potassium current, IK1, considered as the barium sensitive current and the transient outward current, Ito, were recorded in isolated mouse atrial cardiomyocytes using perforated patch-clamp technique.

Results. There was a higher atrial vulnerability to AF in HFD compared to ND mice as indicated by the significant increased duration of AF episodes (values). The plateau phase recorded in ND mice APs disappeared in the majority of HFD mice APs. Moreover, AP duration (APD) measured at 90% of repolarization was significantly reduced in HFD compared to ND LA. Next, we examined the role of ATP-regulated potassium channel (KATP) in the AP shortening of obese mice. In HFD LA, the plateau phase of the AP could be restored by the glibenclamide application, a selective KATP channel blocker, whereas, this plateau phase of the AP observed in ND LA disappeared with cromakalim application, a selective KATP channel opener. Finally, potassium currents recording in isolated atrial myocytes has shown no difference in the global steady-state potassium current whereas Ito was reduced in HFD cardiomyocytes. IK,ATP was increased in HFD myocytes whereas the outward component of IK1 was dramatically reduced and almost absent in HFD myocytes.

Conclusions. Obesity in mice is associated with the shortening of the atrial AP which appears to result from increased activity of KATP-regulated currents and the imbalance of repolarizing potassium currents. Drastic changes in myocardial metabolisms and ATP production in obese mouse heart will be discussed. Shortening of AP duration could contribute to the high vulnerability to AF during obesity.