Abstract: P931

Long-term effects of transient intermittent negative upper airway pressure on atrial remodeling in a novel rat model for obstructive sleep apnea

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Obstructive sleep apnea (OSA) is associated with increased occurrence of atrial fibrillation (AF). Obstructive respiratory events lead to transient hypoxia (IH) and ineffective inspiration against the occluded upper airways result in intrathoracic pressure changes and increasing cardiac transmural pressure gradients.

Objectives: To develop a novel AF animal model mimicking long-term effects of repeated transient intrathoracic pressure changes on top of IH.

Method: In spontaneously breathing sedated rats (2% isoflurane), IH (n= 9) was applied by intermittent increase in the respiratory dead volume. Reproducible and standardized obstructive respiratory events were induced by defined intermittent negative upper airway pressure (INAP = inverse CPAP) applied via a customized mask which was connected to a negative pressure device (n= 9). One minute of IH or INAP was followed by a rest period of nine minutes for four hours every second day. Rats with comparable anesthesia were used as controls (CTR). After three weeks the animals were sacrifice.

Result: Blood pressure and end-diastolic left ventricular pressure were not affected by IH or INAP. Intermittent desaturation (= 77% O2) and post-apneic hyperventilation was comparable in INAP- and IH-rats, but INAP-rats showed significantly higher breathing efforts during apnea compared to IH-rats. Left atrial (LA) interstitial fibrosis formation (+135% vs. CTR, p=0.01) and LA- myocyte diameters (+107%, p=0.03 vs. CTR) were increased in INAP-rats, but unchanged in IH-rats. This was associated with longer inducible AF-durations in INAP-rats (p=0.02 vs. CTR; INAP: 11.65 seconds; CTR: 0.98 seconds) but not in IH-rats (p=0.31 vs. CTR; IH: 1.28 seconds).

Conclusion: Long-term exposure to transient INAP in rats mimics important components of OSA beyond IH and allows the study of the progressive arrhythmogenic substrate in the atrium independent of the development of hypertension or overt diastolic dysfunction.