Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder which is characterized by recurrent occurrence of partial or complete closure of the upper airway during sleep, despite ongoing efforts to breathe. The majority of patients with OSA remain undiagnosed since most of them only come to the attention of a clinician when they complain of daytime sleepiness or when their bed partners report loud snoring or witnessed apnea episodes. Epidemiological studies have indicated that OSA affects 6-13% of the adult population. OSA is multifactorial disease, also considered as a metabolic syndrome, which diagnosis in early stages is challenging due to its presentation. Recently, sound connection between transthyretin (TTR) protein modifications present in human plasma samples and appearance of sleep apnea syndrome has been established. Mass Spectrometric Immunoassay (MSIA) was successfully applied previously on identification of and quantification of TTR variants present in human serum. We took advantage on this powerful method to investigate possible modifications of TTR proteoforms in patients with OSA.

**Methods**

**Results and Discussion**

**Impact of Sleep Apnea**

1. Typical MS spectra of TTR proteoforms originating from human plasma samples..

2. Differences of TTR proteoforms in function of OSA severity in the samples collected in evening: a) TTRn, b) TTRCysGly, c) dTTRs and e) dTTRn.

3. Linear dependence of TTR proteoforms on RDI in function of OSA severity: a) TTRn, b) TTRCysGly, c) dTTRs and e) dTTRn.

4. Linear dependence of evening-morning difference of TTR proteoforms on RDI in function of OSA severity: a) TTRn, b) TTRCysGly, c) dTTRs and e) dTTRn.

**Conclusion**

Obstructive sleep apnea (OSA) is an underdiagnosed common public health concern causing deleterious effects on metabolic and cardiovascular health. Standard for diagnosis is polysomnography and it can be only done in hospitals and specialized sleep clinics. Recent studies found connection between TTR protein modifications present in human plasma samples and appearance of sleep apnea syndrome. In our work we investigated expression of TTR proteoforms in individuals with different severity of OSA. This findings revealed that before sleep 5 of totally 6 identified TTR variants are significantly decreased compared to control snorers. While cysteyl-glycine modification (TTRCysGly) has strong significance in differentiating OSA severity. Analysis of morning samples revealed that TTR modifications are triggered during sleep resulting in balanced levels of TTR proteoforms between all groups. Both, evening levels of individual TTR variants and evening-morning difference have significant influence on RDI. However, change in TTRCysGly expression is highlighted because it significantly correlates with RDI values, OSA severity and abdominal perimeter. This findings make TTRCysGly new putative biomarker for screening of OSA patients and potentially great addition to further OSA diagnosis. To validate obtained results MSIA-TTR analysis on large cohorts are needed. Pathophysiological mechanisms behind these changes on TTR is still to be elucidated.

**References**