Background: Obstructive sleep apnea (OSA) has been increasingly linked to cardiovascular diseases and endothelial dysfunction. Methylated arginines, endogenous inhibitors of nitric oxide synthase, have been implicated as a possible mechanism for endothelial dysfunction in cardiovascular diseases. We tested the hypothesis that repetitive severe hypoxia/ hypercapnia resulting from upper airway occlusion causes asymmetrically methylated arginines (asymmetric dimethylarginine, ADMA, and monomethylarginine, L-NMMA).

Methods: We studied 10 men with newly diagnosed OSA who were free of other diseases and had never been treated for OSA and were taking no medications. Measurements were made before and after 5 hours of untreated OSA, and again after 4 hours of acute continuous positive airway pressure (CPAP) treatment. We compared methylated arginine measurements in these patients to measurements obtained at similar times in 10 matched control subjects.

Results: Baseline ADMA and L-NMMA levels before sleep were similar in the OSA and control group. ADMA and L-NMMA levels increased significantly (from 13.9±0.7 to 16.1±0.5, P=0.03, and from 4.6±0.2 to 5.5±0.1 ng/ml, P=0.002, respectively) in the OSA group after 5 hours of untreated OSA. The increase in ADMA and L-NMMA was blunted by acetylcysteine CPAP treatment. There was a significant correlation between Apnea-Hypopnea Index and increases in ADMA (P=0.00, R=0.77) and L-NMMA (P=0.00, R=0.62). In the control group, methylarginine levels were stable throughout the night.

Conclusions: OSA is associated with acute elevation of ADMA and L-NMMA. This increase is blunted by effective CPAP treatment. Increased asymmetrically methylated arginines may be a potential mechanism to explain the association between OSA and cardiovascular disease.

11:30 a.m.