# INTERMITTENT HYPOXIA IMPAIRS ENDOTHELIAL FUNCTION IN EARLY, RATHER THAN IN ADVANCED ATHEROSCLEROSIS

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**Background:** Intermittent hypoxia seems to be a major pathomechanism of obstructive sleep apnea underlying progression of atherosclerosis. Goal of our study was to prove if hypoxia-induced vasculopathy depends on the initial stage of atherosclerosis.
**Methods:** 16 ApoE-/- mice were exposed to a 6-week-intermittent hypoxia (21-5% FiO(2), 33 cycles, 8h/day) immediately (early atherosclerosis, n=8) or after 5 weeks of high-cholesterol diet (advanced atherosclerosis, n=8). Remaining 16 ApoE-/- mice under normoxia served as corresponding controls. All animals were fed high-cholesterol diet during the whole experiment. Endothelial-dependent vessel relaxation was measured by means of an organ bath technique. Blood plasma CD31+/annexin V+ endothelial microparticles as well as sca1/flk1+ endothelial progenitor cells in blood and bone marrow were analyzed by flow cytometry. Levels of reactive oxygen species in aorta were evaluated by L-O12-enhanced chemiluminescance.
**Results:** Intermittent hypoxia impaired endothelial function (56.6±6.2% of maximal phenylephrine-induced vasoconstriction vs. control: 35.2±4.1%) and integrity (percentage of endothelial microparticles: 0.3±0.04% vs. control: 0.1±0.02%, resp., $p<0.05$) in early atherosclerosis. This observation could be explained due to the attenuated peripheral repair capacity expressed as decreased number of endothelial progenitor cells in blood (2.0±0.5%, 5.3±1.5%, resp., $p<0.05$) despite increased number of these cells in the bone marrow (2.0±0.4%, 1.1±0.2%, resp., $p<0.05$) and the higher levels of free radicals under hypoxia ($p<0.05$). In contrast, endothelial function, as well as microparticle and endothelial progenitor cell levels were similar under hypoxia vs. control in advanced atherosclerosis.
**Conclusions:** Hypoxia aggravates endothelial dysfunction and destruction in early, but not advanced atherosclerosis.