

## **Doktorsavhandling -**

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**Institution:** Department of Clinical Pharmacology ; Avdelningen för klinisk farmakologi

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**Abstract:** This thesis addresses the association between sleep disordered breathing (SDB) and hemodynamic function. A cross sectional study in a sleep laboratory cohort (n=1190) demonstrated a dose-response relationship between the severity of SDB, expressed as respiratory disturbance index (RDI), and office blood pressure, heart rate, and the risk of hypertension. This association was independent of confounding factors like age, Body Mass Index (BMI), and gender. Men aged 50 years or below seemed to be more susceptible for the association between SDB and hypertension. The control of hypertension was assessed in a subgroup of 599 previously diagnosed hypertensive patients. RDI was increased in patients with an actual blood pressure exceeding 160/95 mmHg, defined as uncontrolled hypertension. Elevated blood pressure was also associated with age and BMI. In multivariate analysis RDI and age were the only significant predictors for uncontrolled hypertension in younger patients. Hemodynamic function during supine bicycle exercise testing was assessed in 1149 patients of the sleep laboratory cohort. Maximal load tended to decrease by every RDI unit in multivariate analysis. The heart rate response was reduced by SDB activity in a dose related manner. The increase in peripheral arterial resistance after adrenergic  $\alpha$ -receptor stimulation with norepinephrine (NE), assessed with forearm venous plethysmography, was attenuated in normotensive patients with obstructive sleep apnea (OSA). The relative increase in resistance following NE was lower in the OSA group and negatively correlated with resting plasma NE concentration. In addition, there was a reduced vascular response to  $\beta_2$ -adrenoreceptor stimulation with isoproterenol. The results suggest a functional downregulation of vascular  $\alpha$ - and  $\beta_2$ -receptors. A fingerplethysmographic device was designed to assess changes in digital blood flow by analysis of pulse wave amplitude (PWA). Arousal following SDB were associated with a markedly reduction in PWA. Fingerplethysmography was provided a tool for continuous non-invasive assessment of changes in  $\alpha$ -receptor mediated vasoconstriction in the digital vascular bed and may characterise autonomic activation during disturbed sleep. In conclusion, SDB is associated with acute, intermediate and long-term hemodynamic dysfunction. The high prevalence of cardiovascular disease in SDB patients provides support for consideration of SDB in diagnostic and therapeutic procedures related to cardiovascular disease.