

# Obstructive Sleep Apnea in Coronary Artery Disease: Impact of CPAP treatment

Akademisk avhandling

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- I Peker Y, Glantz H, Thunström E, Kallryd A, Herlitz J, Ejdebäck J. Rationale and design of the Randomized Intervention with CPAP in Coronary Artery Disease and Sleep Apnoea - RICCADSA trial. *Scand Cardiovasc J* 2009; 43:24-31.
- II Glantz H, Thunström E, Herlitz J, Cederin B, Nasic S, Ejdebäck J, Peker Y. Occurrence and Predictors of Obstructive Sleep Apnea in a Revascularized Coronary Artery Disease Cohort. *Ann Am Thorac Soc* 2013; 10: 350-356.
- III Glantz H, Thunström E, Johansson MC, Wallentin Guron C, Uzel H, Ejdebäck J, Nasic S, Peker Y. Obstructive sleep apnea is independently associated with worse diastolic function in coronary artery disease. *Sleep Med* 2015; 16:160-167.
- IV Glantz H, Johansson MC, Thunström E, Wallentin Guron C, Uzel H, Saygin M, Herlitz J, Peker Y. Effect of Positive Airway Pressure on Diastolic Function in Coronary Artery Disease Patients with Non-Sleepy Obstructive Sleep Apnea. *In manuscript*
- V Peker Y, Glantz H, Eulenburg C, Wegscheider K, Herlitz J, Thunström E. Effect of Positive Airway Pressure on Cardiovascular Outcomes in Coronary Artery Disease Patients with Non-Sleepy Obstructive Sleep Apnea: The RICCADSA Randomized Controlled Trial. *Am J Respir Crit Care Med*. 2016 Feb 25. [Epub ahead of print]



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# Obstructive Sleep Apnea in Coronary Artery Disease: Impact of CPAP treatment

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## ABSTRACT

*Background:* Obstructive sleep apnea (OSA) is common in patients with coronary artery disease (CAD). Earlier research has not investigated whether CAD patients should be screened for OSA and subsequently treated with continuous positive airway pressure (CPAP) even if they have no symptoms. This thesis investigated the prevalence and predictors of OSA in a newly revascularized CAD cohort, and further addressed the relationship between OSA and diastolic dysfunction among patients with left ventricular ejection fraction (LVEF)  $\geq 50\%$ . Moreover, the impact of CPAP treatment on diastolic function as well as on long-term cardiovascular outcomes was evaluated in patients with CAD and non-sleepy OSA.

*Methods:* Patients who underwent a mechanical revascularization in Skaraborg, Sweden, between September 2005 and November 2010 ( $n=1,291$ ) were invited to participate. Anthropometrics and medical history were obtained, ambulatory sleep recording was performed, and all subjects completed the Epworth Sleepiness Scale (ESS) questionnaire. OSA diagnosis was based on an apnea-hypopnea index (AHI)  $\geq 15/h$ , and no OSA was defined as an AHI  $< 5/h$ . Left atrial diameter, myocardial relaxation velocity ( $\dot{e}$ ), and the ratio of early diastolic mitral flow to myocardial relaxation velocity ( $E/\dot{e}$ ) (were evaluated as echocardiographic diastolic function parameters at baseline, three months, and one year. The long-term primary endpoint was the first event of new revascularization, myocardial infarction, stroke or cardiovascular death. Intention-to-treat (ITT) and on-treatment analyses were performed for evaluation of the impact of CPAP in the randomized controlled arm of the CAD patients with non-sleepy OSA (ESS score  $< 10$ ).

*Results:* OSA was found among 422 of the 662 study participants (64%), of whom 62% were non-sleepy. The prevalence of OSA was higher than the prevalence of obesity, hypertension, diabetes, and current smoking. In the subgroup of patients with preserved LVEF, worse diastolic function was more common in the OSA group (54% vs 41%,  $p=0.019$ ). OSA was significantly associated with worse diastolic function after adjustment for confounding factors. Regarding the impact of CPAP treatment, there was no significant improvement in any of the diastolic function parameters in non-sleepy OSA patients in the ITT analysis. Neither were long-term adverse outcomes reduced significantly in the ITT population ( $n=244$ ) during a median follow-up of 57 months. In the on-treatment analysis, CPAP usage of at least four hours per night was associated with an increase in  $\dot{e}$  tissue velocity after adjustment for the confounding factors (odds ratio 2.3, 95% confidence interval (CI) 1.0–4.9;  $p=0.039$ ). This level of CPAP usage was associated also with a risk reduction (hazard ratio 0.29; 95% CI 0.10–0.86;  $p=0.026$ ) in long-term adverse outcomes after adjustment for the baseline comorbidities.

*Conclusions:* The prevalence of unrecognized OSA in this CAD cohort was higher than previously reported, and OSA was associated with worse diastolic function among patients with preserved LVEF. Routine prescription of CPAP to CAD patients with non-sleepy OSA had no beneficial impact on diastolic function and long-term outcomes in the ITT population. However, there was a significant risk reduction after adjustment for baseline comorbidities and CPAP adherence. These findings need to be further explored in larger clinical cohorts with more homogeneous CAD populations.