

## Sleep apnea and atrial fibrillation: cause or comorbidity?

Akademisk avhandling

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av

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### Avhandlingen baseras på följande delarbeten

- I Holtstrand Hjälms, H, Hansson, PO, Fu, M, Mandalenakis, Z, Thunström, E. Association between obstructive sleep apnea and atrial fibrillation in a general population sample of 71-year-old men.  
*Submitted to Journal of Sleep Research 2023*
- II Holtstrand Hjälms, H, Fu, M, Hansson, PO, Zhong, Y, Caidahl, K, Mandalenakis, Z, Morales, D, Ergatoudes, C, Rosengren, A, Grote, L, Thunström, E. Association between left atrial enlargement and obstructive sleep apnea in a general population of 71-year-old men.  
*J Sleep Res. (2018) 27, 254–260. doi: 10.1111/jsr.12585*
- III Holtstrand Hjälms, H, Thunström, E, Glantz, H, Karlsson, M, Celik, Y, Peker, Y. Obstructive sleep apnea severity and prevalent atrial fibrillation in a sleep clinic cohort with versus without excessive daytime sleepiness.  
*Sleep Medicine 112 (2023) 63–69. doi.org/10.1016/j.sleep.2023.09.012*
- IV Holtstrand Hjälms, H, Thunström, E, Glantz, H, Karlsson, M, Peker, Y. Association between obstructive sleep apnea and incident atrial fibrillation in a sleep clinic cohort.  
*Manuscript*
- V Peker, Y, Holtstrand-Hjälms, H, Celik, Y, Glantz, H, Thunström, E. Postoperative Atrial Fibrillation in Adults with Obstructive Sleep Apnea Undergoing Coronary Artery Bypass Grafting in the RICCADSA Cohort.  
*J.Clin. Med. 2022,11,2459. doi: 10.3390/jcm11092459*

SAHLGRENKA AKADEMIN  
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# Sleep apnea and atrial fibrillation: cause or comorbidity?

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## ABSTRACT

**Background:** Obstructive sleep apnea (OSA) and atrial fibrillation (AF) are common conditions, associated with morbidity and mortality. Both OSA and AF often go undetected. It has been suggested that OSA may be a modifiable risk factor for AF development. OSA has been linked with AF prevalence in general cohorts and with enlargement of the atria in sleep lab cohorts. In addition, OSA has been associated with postoperative AF (POAF) after coronary artery bypass graft (CABG) in coronary artery disease (CAD) cohorts.

**Aims:** The papers described in this thesis aim to address the following issues: (1) the association between OSA and AF prevalence, (2) the association between OSA and left atrial enlargement in a general population, (3) whether OSA severity and excessive daytime sleepiness (EDS) were associated with AF, (4) whether OSA severity was associated with OSA incidence in a sleep clinic cohort, and (5) whether OSA was associated with POAF in a CAD cohort.

**Methods and Results:** This thesis consists of five papers, with data from three cohorts. Paper I and paper II are based on the longitudinal cohort "The Study of Men Born in 1943", consisting of a random sample of men from the general population living in Gothenburg, Sweden, recruited in 1993. In 2014, the 653 remaining men were invited to a re-examination, of whom 536 participated. This re-examination included a physical examination, ECG, two-week thumb ECG, a home sleep apnea test (HSAT), an echocardiographic examination, and questionnaires. The 412 participants with complete data from the HSAT were included. Paper I showed that AF is much more common among men with severe OSA compared to men with no, mild, or moderate OSA. While the association with severe OSA was found to be significant in adjusted analyses, it may be mediated by known confounding factors, mainly heart failure. Paper II showed an independent linear association between left atrial enlargement and OSA severity. Paper III and paper IV are based on the "Sleep Apnea Patients in Skaraborg" cohort. All consecutive patients referred to the sleep clinics at Skaraborg Hospital in southwestern Sweden between January 2005 and December 2011 were included. Patients were screened using HSAT and they filled out questionnaires concerning EDS. Follow-up of comorbidities, through review of hospital records ended in April 2018. A total of 4239 adult patients were included in the cohort. Paper III showed an independent association between severe OSA and AF prevalence in OSA patients without EDS. In paper IV, OSA severity was associated with shorter survival free time concerning AF incidence, and moderate and severe OSA were associated with AF incidence in unadjusted analyses. In adjusted analyses, this association was no longer significant, indicating that heart failure and age are major confounders and are involved in AF incidence. Paper V is a secondary analysis of data from the Randomized Intervention with Continuous Positive Airway Pressure (CPAP) in Coronary Artery Disease and Obstructive Sleep Apnea (RICCADSA) trial. This secondary trial includes 147 patients who underwent HSAT after CABG between December 2005 and November 2010. Paper V showed a linear association between OSA severity and POAF within 30 days, and severe OSA was significantly associated with POAF.

**Conclusions:** OSA severity, and foremost severe OSA, was associated with AF prevalence and left atrial enlargement in a general male population. In our sleep clinic cohort, severe OSA without EDS was associated with AF, a patient group for which CPAP treatment may be challenging. Severe OSA was associated with AF in the survival analyses. Furthermore, severe OSA was associated with AF after CABG. Overall, severe OSA was associated with worse outcomes when compared to patients with no, mild, or moderate OSA. AF or POAF was more prevalent in patients with severe OSA in all cohorts.

**Keywords:** Obstructive sleep apnea, atrial fibrillation, excessive daytime sleepiness

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