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SLEEP-RELATED HYPOXEMIA ASSOCIATION WITH INCIDENT ATRIAL FIBRILLATION IN A CLINIC-BASED COHORT

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Introduction: Sleep disordered breathing (SDB) has been implicated in atrial fibrillation (AF) in population-based studies, however, its role remains unclear and inconsistent. We hypothesize greater risk of 5-year incident AF with SDB and sleep-related hypoxia in a clinic-based cohort.

Methods: Cleveland Clinic patients (age>18) who underwent polysomnogram (PSG) or split studies 11/27/2004-12/30/2015 with >3 hours diagnostic time were examined. Predictors include AHI, % sleep time oxygen saturation<90% (T90), and minimum and mean oxygen saturation(minSaO2 and meanSaO2, respectively). Cox proportional hazard models were fit with time from sleep study to AF diagnosis as the dependent variable. Covariates included age, sex, race, body mass index(BMI), cardiovascular risk factors (hypertension, diabetes mellitus, hyperlipidemia), heart failure, coronary artery disease, myocardial infarction, history of coronary artery bypass grafting, chronic obstructive pulmonary disease, tobacco use, and use of anti-arrhythmic drugs. Data were censored at date of last follow up or at 5-years.

Results: The sample was comprised of 43,634 patients: age 51.7±14.5, 51.9% male, 74.5% White, and 7.1%(n=3,090) with AF. Of those without AF, 1,176(2.9%) developed 5-year incident AF. For each 10% increase in T90, incident AF increased by 7% (HR=1.07, 95%CI=1.05-1.10). Compared to reference, patients with 25.01-50%, 50.01-75%, and 75.01-100% time T90 had 22% (HR=1.22, 95%CI=1.01-1.46), 49% (HR=1.49, 95%CI=1.20-1.85), and 65% (HR=1.65, 95%CI=1.26-2.15) higher incident AF, respectively. For every 10-unit increase in minSaO2 and meanSaO2, incident AF decreased by 11%(HR=0.89, 95%CI=0.83-0.95) and 23% (HR=0.77, 95%CI=0.68-0.86), respectively. AHI did not demonstrate a statistically significant relationship with incident AF at a significance level of 0.05.

Conclusion: Sleep-related hypoxemia, defined by cumulative burden below 90% SaO2, demonstrated an association with incident AF in this large clinic-based cohort, even considering confounding factors. On the other hand, SDB severity as defined by AHI did not demonstrate this relationship. These findings are consistent with experimental models that identify intermittent hypoxia and oxidative stress leading to alterations of the cardiac substrate, thus implicating sleep-related hypoxemic mechanisms as a salient driver in the evolution of atrial arrhythmogenesis.

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MEDIATION OF BIOMARKERS OF INFLAMMATION IN SLEEP-RELATED HYPOXIA AND COVID-19 CLINICAL OUTCOMES

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Introduction: Central to the pathophysiology of SARS-CoV-2 is immune dysregulation and systemic inflammation, however, it is

yet unknown whether sleep-related hypoxemia--which we have recently noted to be associated with worse COVID-19 clinical outcomes--is mediated by these biomarkers and pathways.

Methods: Data from patients who tested positive for SARS-CoV-2 and part of the integrated Cleveland Clinic COVID-19 and sleep laboratory registries from March-November 2020 were included. To assess the mediation effect of biomarkers, the relationship between sleep-related hypoxia measures (% sleep time<90%SaO2, T90) and moderate/severe WHO-7 COVID-19 score (use of supplemental oxygen, non-invasive ventilation, mechanical ventilation/ECMO or death) was first tested. The mediation effect, or natural indirect effect, of biomarkers of inflammation (C-Reactive Protein (CRP), white blood cell (WBC) count (with a focus on lymphocyte count) and lactate) was then estimated by logistic regression models adjusted for demographics, comorbidities, smoking pack year and site location using PROC CAUSALMED statement in SAS software (version 9.4, Cary, NC).

Results: The analytic sample included 446 patients hospitalized due to COVID-19: age:63.3±13.8 years, 51.3% female, 39% African American with body mass index(BMI)=36.1±9.3kg/m². Thirty-six percent used supplemental oxygen, 4% used high-flow or non-invasive ventilation, 5% required ECMO or mechanical ventilation and 2% died. Hypoxic measures were associated with moderate/severe WHO-7 COVID-19 outcome: T90 median (>1.8%vs.≤1.8%) (OR=2.04, 95%CI:1.28-3.23, p=0.003), 5% increases in both mean SaO2 (OR=0.43, 95%CI: 0.26-0.70, p<0.001) and minimum SaO2 (OR=0.84, 95%CI: 0.72-0.99, p=0.03). CRP was associated with mean SaO2 (p=0.040) and minimum SaO2 (p=0.029), likewise mediation analysis showed that there was a significant natural indirect effect of CRP in both hypoxia measures (OR=0.86, 95%CI 0.73-0.99, p=0.036; OR=0.95, 95%CI 0.90-1.00, p=0.034 respectively). WBC count, but not lymphocyte count subset, was associated with mean SaO2 (p=0.044), but the natural indirect effect was not significant (p=0.23). Lactate was associated with minimum SaO2 (p=0.044), but the natural indirect effect was not significant (p=0.23). T90 median was not associated with CRP (p=0.13), WBC count (p=0.87) or lactate (p=0.28).

Conclusion: CRP appears to represent a relevant mediator of sleep-related hypoxia and WHO-7 clinical outcomes. Further investigation is needed to elucidate if treatment of sleep-related hypoxia downregulates biomarkers of systemic inflammation to modify disease course.

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POLYSOMNOGRAM CHARACTERISTICS ASSOCIATED WITH ARTIFICIAL INTELLIGENCE ENABLED ELECTROCARDIOGRAM ALGORITHM PREDICTED PROBABILITY OF ATRIAL FIBRILLATION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is associated with atrial fibrillation (AF). Several features of OSA are thought to play role in the development of AF. A recently developed artificial intelligence (AI) enabled electrocardiogram (ECG) algorithm predicts the probability of future development of AF from a single ECG. We sought to examine the relationship between polysomnogram (PSG) and clinical features of patients with OSA and the probability of future AF (P-AF).

Methods: Consecutive adults (age ≥ 18) with OSA and with an ECG obtained within 2 years of their attended polysomnograms (PSG)