Association Between Polysomnographic Phenotypes of Obstructive Sleep Apnea and Incident Type 2 Diabetes

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BACKGROUND

- Obstructive sleep apnea (OSA) is associated with increased risk for adult type 2 diabetes (T2DM) cardiovascular disease (CVD).
- The specific linking mechanism between T2DM and OSA has yet to be fully described, and a better characterization of OSA subgroups at higher risk for T2DM is needed.
- Drs. Zinchuk, Yaggi & their team previously identified seven unique OSA polysomnographic phenotypes that were shown to be associated with a substantially changed degree of risk for incident CVD and death.
- Concerning T2DM risk, we know little about the relationship of these polysomnographic phenotypes.

RESEARCH HYPOTHESIS

Our hypothesis: Combinations of simple, available, abstracted polysomnographic metrics (identified as phenotypes/clusters via cluster analysis) can aid in identifying OSA adults at greatest risk for T2DM.

OBJECTIVES

1) To discover differences in T2DM incidence rates using the seven polysomnographic phenotypes:
   - 1. **Mild**, 2**. Periodic Limb Movements of Sleep (PLMS)**, 3. **Non-Rapid Eye Movement (NREM) and Poor Sleep**, 4. **Rapid-Eye Movement (REM) and Hypoxia**, 5. **Hypopnea and Hypoxia**, 6. **Arousal and Poor Sleep**, and 7. **Combined Severe**.
2) To compare polysomnographic baseline features with the clinical characteristics (differences) throughout polysomnographic phenotypes/clusters.
3) To examine if polysomnographic phenotypes associate with incident T2DM in an adult cohort during OSA evaluation.

METHODS

Study Design and Sample

- Retrospective secondary data analysis of the Determining Risk of Vascular Events by Apnea Monitoring (DREAM) study.
- Sample: A US veteran cohort with suspected OSA but without baseline diabetes (**N=840**).
- Cohort derived from three VA medical centers (West Haven, Connecticut; Indianapolis, Indiana; and Cleveland, Ohio) and enrolled from 2000-2004 with follow-up through 2012.

Definition of Incident T2DM

- Absence of known diabetes at baseline but a fasting glucose level >126 mg/dL plus a new diabetes diagnosis during the follow-up period.

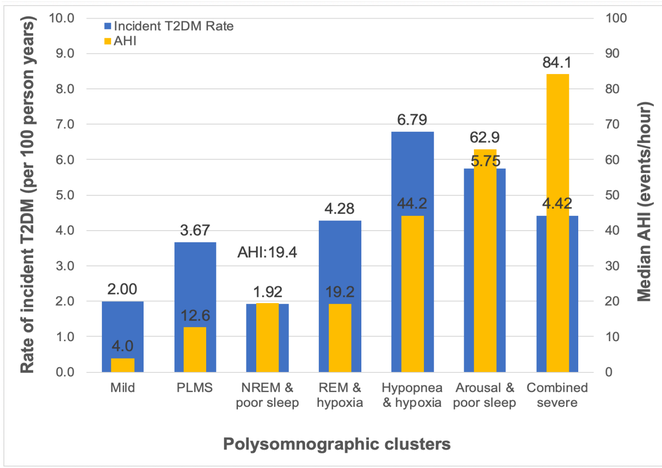
Data Analysis

- Incidence rate of T2DM: The rate was calculated as number of patients with T2DM in each phenotype divided by total number of patient-years under observation. This was then expressed as number of events per 100 patient-years.
- Unadjusted and adjusted Cox proportional hazards regression: Both were used to examine the longitudinal relationship between the polysomnographic phenotypes and incident T2DM.

RESULTS

- 122 (14.5%) patients developed incident T2DM in 61 months, the median follow-up period (incidence rate 3.0 per 100 person-years).
- The incident new-onset T2DM rate varied according to polysomnographic phenotype. Highest to lowest: “hypopnea & hypoxia” phenotype, “arousal and poor sleep”, “combined severe”, “rapid-eye-movement and hypoxia”, “PLMS”, “mild” and “non-rapid eye movement and poor sleep”.

Figure 1. Rates of Incident T2DM, Stratified by Polysomnographic Phenotypes/Clusters.

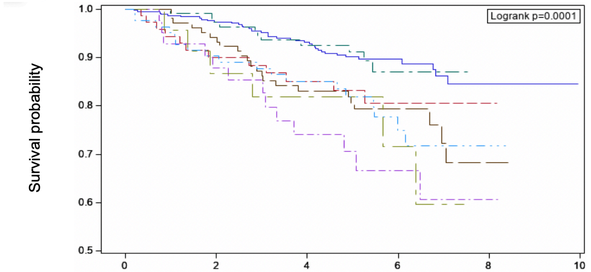


Note: PLMS= periodic limb movements of sleep; NREM=non-rapid eye movement; REM=rapid-eye movement.

Baseline Characteristics of Polysomnographic Phenotypes

- **Mild**: The lowest AHI, greater sleep efficiency, a higher percentage of REM sleep
- **PLMS**: The highest PLMS index and a low respiratory event frequency (AHI 12.6 events/hr)
- **NREM & poor sleep**: An impaired sleep architecture with events in NREM sleep but minimal hypoxia
- **REM & hypoxia**: A preserved sleep but respiratory events in REM sleep with a higher burden of hypoxia
- **Hypopnea & hypoxia**: 9 out of 10 events were associated with a ≥4% desaturation and a high burden of hypoxia
- **Arousal & poor sleep**: Apnea with arousals only dominated, markedly disturbed sleep
- **Combined severe**: Markedly high AHI, highest percent combined apneas with most severe burden of hypoxia

Figure 2. Kaplan-Meier Curves for the Association of Polysomnographic Phenotypes and Incident T2DM



Mildest	395	363	299	106	8	0
PLMS	73	59	48	18	1	0
NREM & poor sleep	115	107	91	31	0	
REM & hypoxia	107	97	76	38	4	0
Hypopnea & hypoxia	43	35	24	11	3	0
Arousal & poor sleep	24	18	16	6	0	
Combined severe	83	73	62	27	2	0

Following adjustment for baseline risk factors, hazard ratios were definitively increased for “hypopnea and hypoxia” (3.18 [95% CI: 1.53 to 6.61]) &“PLMS” (2.26 [95% CI: 1.06 to 4.83]) phenotypes vs. the “mild”.

LIMITATIONS

- Retrospective design; criteria for DM definition.
- Non-inclusion of other metrics of physiological sleep disturbances such as hypoxic burden.

CONCLUSIONS

- T2DM incidence rates vary according to polysomnographic phenotypes in a veteran cohort.
- “Hypopnea and hypoxia” and “PLMS”, two polysomnographic phenotypes, associated independently with increased risk of T2DM.

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