

SHHS MANUSCRIPT PROPOSAL
ARIC MANUSCRIPT PROPOSAL # 886S

PC REVIEWED: 06/18/02

STATUS: A

PRIORITY:

SC REVIEWED: 06/18/02

STATUS: A

PRIORITY:

1. FULL TITLE:

Retinal microvascular abnormalities and sleep-disordered breathing

ABBREVIATED TITLE:

2. PROPOSED WRITING GROUP MEMBERS:

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3. TIMELINE [TARGET START AND FINISH DATES]

Analysis of ARIC data could begin immediately; will need to obtain CHS retinal data from CHS investigators. Analysis and preliminary draft to be completed by October 2002.

4. RATIONALE:

Recently published data from SHHS demonstrate a cross-sectional relation between sleep-disordered breathing (SDB) and overt cardiovascular disease (1), but it is unknown whether SDB is associated with pathology of the microvasculature. Detection of microangiopathy *in vivo* can be accomplished non-invasively with retinal photography, which was a component of clinic visit examinations in both the ARIC and CHS cohorts.

Retinal microvascular abnormalities occur primarily as a result of hypertension, aging, or other adverse vascular changes. Since SDB has been associated with hypertension in the SHHS cohort (2), one would expect to observe a relation between retinal abnormalities and SDB that is mediated by hypertension. However, it is plausible that independent of hypertension, SDB may be related to microvascular disease via other mechanisms (e.g. endothelial dysfunction that may be the result of chronic nocturnal hypoxemia). Recent clinical studies by Kraiczi (3) and Kato (4) have demonstrated impaired endothelial-dependent vasomotor regulatory functions in apneics.

Determining whether SDB is associated with microvascular retinopathy would serve to establish a link between SDB and early, subclinical vascular disease. In addition, demonstrating an association between SDB and retinal microvascular disease that is independent of hypertension could provide further support for a non-hypertension-mediated etiologic pathway between SDB and cardiovascular disease that may have its origin in hypoxemia-related endothelial dysfunction or injury.

Both ARIC and CHS utilized the same retinal reading center (University of Wisconsin) so the evaluation and scoring of retinal photographs was similar across studies. We propose here a local analysis of the relation between SDB and retinal microvascular abnormalities among the ARIC and CHS participants of SHHS.

5. HYPOTHESES

- 1) The prevalence of retinal abnormalities increases with increasing respiratory disturbance index and hypoxemia, and if so:

- 2) This association is attenuated, but not nullified, after adjustment for hypertension and other risk factors for retinal abnormalities.

6. DATA [VARIABLES, TIME WINDOW, SOURCE, INCLUSIONS/EXCLUSIONS]

The main dependent variable will be a series of retinal abnormalities including arteriovenous nicking, focal arteriolar narrowing, blot and flame-shaped hemorrhages, microaneurysms, and soft exudates. In addition, a collective endpoint of any of these retinopathies will be derived and examined. Retinal data was collected as part of Visit 3 in ARIC (1993-1995) and as part of the ninth clinic exam (Year 10, years?) in CHS. The primary independent variables will be respiratory disturbance index (RDI) and % of sleep time with oxygen saturation < 90% of baseline (hypoxemia) collected during SHHS-1 (1995-1997). Covariates to be considered are age, gender, field center, body-mass index, hypertension, diabetes, and smoking status. Data analysis will be conducted on all ARIC and CHS subjects participating in SHHS-1 who have PSG data available and have gradeable retinal photographs.

7. TYPE OF STUDY: Secondary

8. TYPE OF PUBLICATION: Manuscript

TARGET JOURNAL:

9. ANALYSIS RESPONSIBILITY: Local

10. BRIEF ANALYSIS PLAN [include list of variables to be used, time frame of data, source of non-SHHS data, and probable statistical methods]

INDEPENDENT VARIABLES: RDI, hypoxemia

DEPENDENT VARIABLES: retinal abnormalities (as stated above)

COVARIATES: age, gender, field center, BMI, hypertension, diabetes, smoking

STRATIFICATION: possibly on hypertension status if number of retinal abnormalities not prohibitively small

PROBABLE STATISTICAL METHODS: tabular methods, multiple logistic regression

11. REFERENCES

1. Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. *Am J Respir Crit Care Med* 2001; 163:19-25.
2. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *JAMA* 2000; 283:1829-36.
3. Kraiczi H, Caidahl K, Samuelsson A, et al. Impairment of vascular endothelial function and left ventricular filling: Association with the severity of apnea-induced hypoxemia during sleep. *Chest* 2001; 119:1085-1091.

4. Kato M, Roberts-Thomson P, Phillips B, et al. Impairment of endothelial-dependent vasodilation of resistance vessels in patients with obstructive sleep apnea. *Circulation* 2000; 102:2607-2610.