1a. Metabolic Predictors of Change in the Respiratory Disturbance Index (RDI)

b. Metabolic Predictors of RDI Change

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3. After completion of Samet manuscript on risk factors for change in RDI.

4. Several studies have suggested that OSA commonly co-exists with a “metabolic syndrome” phenotype. However, little work has been done to determine whether metabolic dysfunction, independently of obesity, is a predictor of incident sleep disordered breathing or increase in RDI.

5. Independently of standard OSA risk factors (e.g., age, BMI, gender), metabolic factors (dyslipidemia, insulin resistance, waist circumference) predict change in RDI, either as a measure of a metabolic syndrome phenotype or through direct pathophysiological mechanisms.

6. Demographic factors, BMI, smoking, alcohol use, disease status, insulin, glucose, lipid levels, medications (specific). Analyses will be restricted to sites that collected fasting blood samples and only the insulin, glucose and lipid levels available closest to the baseline polysomnogram will be used. Individuals with type I diabetes or pancreatic failure will be excluded.

7. Secondary Study

8. Journal Article

9. Central Analysis

10. Introduction

The strong cross-sectional associations between sleep-disordered breathing and such metabolic disorders as insulin resistance and dyslipidemia (Newman et al 2001, Ip et al 2002, Punjabi et al 2002) support the notion that metabolic dysfunction may predict the development of sleep-disordered breathing, either by providing a measure of visceral fat deposition or other obesity pattern not obtained from standard measures of obesity, or through direct causal mechanisms. The Cleveland Family Study has suggested that serum cholesterol level was an independent predictor of the change in RDI over time after adjusting for obesity (Tishler et al 2003). Using the SHHS population, we will consider whether measures of metabolic dysfunction provide additional information in predicting RDI change that can not be obtained from measures of obesity.

11. Brief Analysis Plan (see attached variable list):

The analysis will use the regression models created by the Samet manuscript on “RDI Change Predictors” as a framework although these models may need to be re-assessed for their validity within the restricted dataset for which these analyses will be conducted. To the Samet model, 3 sets of novel risk factors will be added: insulin resistance (fasting insulin and fasting HOMA), dyslipidemia (total cholesterol, HDL, triglyceride levels), and waist circumference. These will be considered both as continuous variables (in which case use of hypoglycemic and lipid-lowering medications will be dealt with as covariates as well as exclusion for sensitivity analysis) as well as discrete variables using clinically relevant cutpoints where
medication use will assign individuals automatically to the highest category. Other covariates will include those variables found by Samet et al to be important predictors. The first set of models will use absolute change in RDI between the two polysomnograms as the outcome variable and will be conducted using multivariate linear regression as well as mixed effects models. The second will consider the shift in RDI across a clinically relevant boundary (e.g., RDI < 5 to RDI > 15) as a discrete outcome. For these analyses directed at charges across specific values, logistic regression would be the initial approach, possibly followed by multinomial or quantile regression. Sensitivity analyses will be performed on all models restricting to only subjects who had a blood sample obtained within 1 year of the baseline polysomnogram.

12. Summary:

We propose a complete analysis of the role of metabolic variables to predict change in RDI independently of obesity measures.

13. References


Ip MSM, Lam B, Ng MMT, Lam WK, Tsang KWT, Lam KSL. Obstructive sleep apnea is independently associated with insulin resistance. Am J Respir Crit Care Med 2002; 165: 670-676.
