Development, Validation, and Assessment of an Ischemic Stroke or Transient Ischemic Attack-Specific Prediction Tool for Obstructive Sleep Apnea

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Background: Screening instruments for obstructive sleep apnea (OSA), as used routinely to guide clinicians regarding patient referral for polysomnography (PSG), rely heavily on symptomatology. We sought to develop and validate a cerebrovascular disease-specific OSA prediction model less reliant on symptomatology, and to compare its performance with commonly used screening instruments within a population with ischemic stroke or transient ischemic attack (TIA). *Methods:* Using data on demographic factors, anthropometric measurements, medical history, stroke severity, sleep questionnaires, and PSG from 2 independently derived, multisite, randomized trials that enrolled patients with stroke or TIA, we developed and validated a model to predict the presence of OSA (i.e., Apnea-Hypopnea Index ≥5 events per hour). Model performance was compared with that of the Berlin Questionnaire, Epworth Sleepiness Scale (ESS), the Snoring, Tiredness, Observed apnea, high blood Pressure, Body mass index, Age, Neck circumference, and Gender instrument, and the Sleep Apnea Clinical Score. *Results:* The new SLEEP Inventory (Sex, Left heart failure, ESS, Enlarged neck, weight [in Pounds], Insulin resistance/diabetes, and National Institutes of Health Stroke Scale) performed modestly better than other instruments in identifying patients with OSA, showing reasonable discrimination in the development (c-statistic .732) and validation (c-statistic .731)

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study populations, and having the highest negative predictive value of all in struments. *Conclusions:* Clinicians should be aware of these limitations in OSA screening instruments when making decisions about referral for PSG. The high negative predictive value of the SLEEP INventory may be useful in determining and prioritizing patients with stroke or TIA least in need of overnight PSG.
Key Words: Ischemic stroke—TIA—Obstructive sleep apnea—Screening.
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Introduction

Obstructive sleep apnea (OSA) occurs commonly in the post-ischemic stroke or transient ischemic attack (TIA) population, affecting 60%-80% of persons after their cerebrovascular event.[1,2] Untreated OSA is an independent risk factor for future vascular events (e.g., stroke, myocardial infarction), may complicate management of vascular risk factors (e.g., hypertension, atrial fibrillation), and increases the risk for mortality in patients with cerebrovascular disease.[3-6] Despite the potential treatment and prognostic implications of discovering whether patients with cerebrovascular disease have comorbid OSA, the condition frequently goes undiagnosed.[5,7] This situation may be due, in part, to the observation that hallmark features of OSA (e.g., excessive daytime sleepiness) can occur less commonly among patients with cerebrovascular disease than in the general population.[5] Several well-validated sleep instruments used in the general population to screen for OSA and perceived somnolence, such as the Berlin Questionnaire (BQ)[8] and Epworth Sleepiness Scale (ESS) score,[6] rely heavily on symptomatic features of OSA, but have not been predictive of OSA (as defined by an Apnea-Hypopnea Index [AHI] ≥5 on polysomnography [PSG]) in mixed stroke populations (ischemic and hemorrhagic).[5,7] A modified version of the Snoring, Tiredness, Observed Apnea, high blood Pressure-Body mass index, Age, Neck circumference, and Gender (STOP-BANG) was only moderately predictive of OSA compared with home sleep testing equipment among patients with a cerebrovascular event,[9,10] whereas the Sleep Apnea Clinical Score (SACS) has not been studied among patients with cerebrovascular disease. Given the suboptimal performance of commonly used OSA screening instruments within the stroke or TIA population, authors have suggested that the development of models based on medical comorbidity should be pursued.[10]

The most recent American Heart Association/American Stroke Association ischemic stroke or TIA prevention guidelines provide new recommendations addressing OSA, noting that PSG might be considered for patients with an ischemic stroke or TIA and, that once diagnosed, treatment of OSA might be considered, given its association with improved post-cerebrovascular event outcomes.[2] The guidelines do not, however, specify which patients should be considered for PSG referral. Because universal OSA screening with PSG may not be feasible based on the worldwide prevalence of stroke, we sought to (1) develop and validate a cerebrovascular disease-specific instrument that would be less reliant on patient symptomatology and anthropometric features, and; (2) determine how well the new instrument, and the BQ, ESS, SACS, and STOP-BANG, predicted the presence and absence of OSA in an exclusively post-ischemic stroke or TIA population (rather than a mixed ischemic and hemorrhagic stroke population). These analyses could then help identify which patients are most (i.e., high positive predictive value [PPV]) or least (i.e., high negative predictive value [NPV]) in need of PSG referral.

Methods

Overview

Participants in 2 separate, multisite, 1-year randomized controlled trials examining the utility of unattended PSG to identify and treat OSA in the post-ischemic stroke or TIA populations with continuous positive airway pressure (CPAP) were used as the study population; the methods of each trial are described elsewhere.[11,12] A clinical prediction model was developed and validated. Results across different OSA prediction instruments were compared.

Patient Populations

From 1 study,[11] Veterans with an ischemic stroke within either 30 days of recruitment or any time after developing a TIA were included as the development cohort, whereas patients (non-Veterans and Veterans) from the second study who had an ischemic stroke or TIA within 1 week of enrollment were included as the validation cohort.[12] Patients enrolled into the study used as the development set had either a history of hypertension or a blood pressure ≥140/90 mm Hg. Both studies used the same exclusion criteria: known history of OSA, suspected sleep disorder other than OSA (e.g., narcolepsy, given that such patients have another indication for formal PSG), life expectancy less than 6 months, inability to use either a nasal or a face mask (as continuous positive airway pressure could not be administered), non–English-speaking patients, and inability to provide informed