

shedding light on Stroke and Sleep

More study is needed about the relationships and significance of OSA, SDB, and stroke.

A 50-YEAR-OLD

man admitted to the hospital with an acute ischemic stroke snored and gasped so loudly while asleep that nearby patients in the stroke unit complained of sleepless nights.

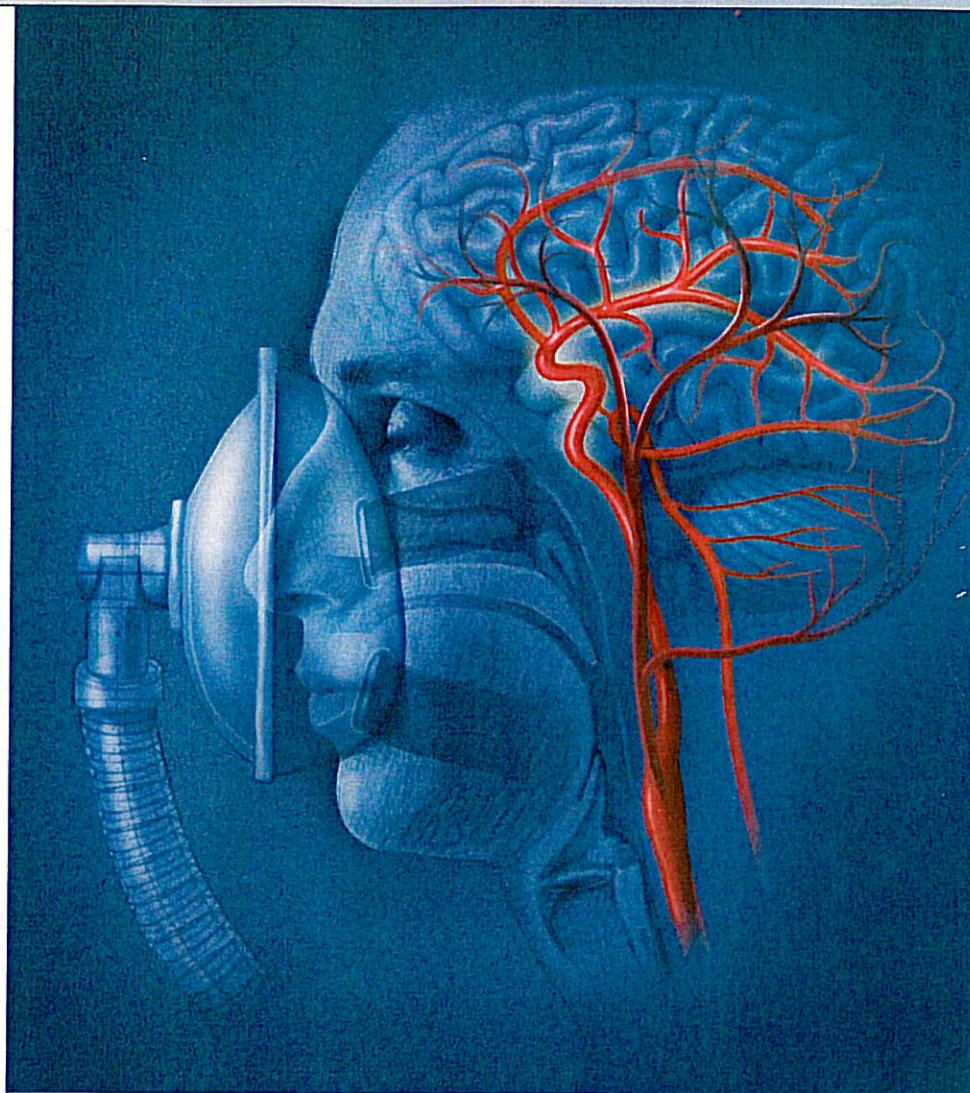
The patient had a history of difficult-to-control hypertension. Since his admission, clinicians observed intermittent atrial fibrillation and intermittent respiratory pauses lasting longer than 20 seconds. Snorts and gasps terminated the pauses, which caused arterial oxygen desaturations in the low 80s on 28 percent F_{iO_2} .

One morning, the patient woke up with a new onset of aphasia, dysphagia, and right-sided weakness. A neurology resident suggested the patient's stroke probably triggered obstructive sleep apnea. However, the family said he has "always snored like that because he's a big man."

When I asked the resident whether we should treat this man for OSA during the acute phase of his stroke, he questioned whether treating the patient would influence the man's long-term stroke outcome.

IN THIS STORY

- Why it is important to increase awareness that OSA is a possible risk factor for stroke and TIA
- How to effectively diagnose and treat OSA and SDB in acute stroke patients

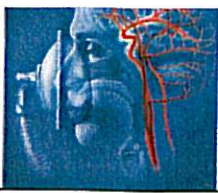


The clinical problem

The most effective strategy for reducing stroke morbidity and mortality is early identification and treatment of stroke risk factors. Most health professionals know that potentially treatable stroke risk factors include hypertension, diabetes mellitus, obesity, heart disease, hyperlipidemia, carotid artery stenosis, tobacco or amphetamine use, physical inactivity, and previous stroke or transient ischemic attack (TIA). However, few know about increasing medical evidence suggesting OSA is an independent risk factor for stroke and TIA.

Clinically significant OSA (defined as 10 or more apneas and hypopneas per hour of sleep [AHI > 10]) has been found in 53 percent to 80 percent of prospective case-control studies of patients with acute first-ever strokes or TIA.¹⁻⁵ Respiratory events in these patients typically are obstructive apneas, although some patients exhibit Cheyne-Stokes or periodic breathing (usually < 6 percent) most often when the first polysomnograph is done within 24 hours of the stroke or when intracerebral hemorrhage caused the stroke.^{6,7,9,10} Central sleep apnea tends to resolve in patients with stroke after the acute stroke period ▶

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stroke and sleep

whereas OSA tends to persist.⁵

Negative prognostic significance of OSA

Several studies have shown that stroke patients with sleep-disordered breathing are more likely to exhibit early neurological worsening, delirium, depressed mood, impaired functional capacity, longer rehabilitation, and long hospital stays.^{1,3,11,12}

Research has identified SDB as an independent prognostic risk factor for death in patients with first-ever stroke.^{13,14} Another prospective study found an AHI > 10 was an independent risk factor for stroke recurrence; 80 percent of patients with recurrent strokes have AHI > 10 vs. 50 percent with first-ever strokes.¹⁵

Patients with acute stroke who also have OSA face an eight-fold increased risk for early neurologic worsening after a first-ever hemispheric stroke.¹ Hypoxic events during sleep predicted a poorer stroke recovery especially among those admitted with more severe strokes.¹¹ Strokes and TIA typically occur in wakefulness between 6 a.m. and noon.¹⁶ However, patients with sleep-onset strokes were more likely to have AHI > 25 per hour of sleep.¹

What predisposes OSA patients to stroke?

Hypertension induced by OSA may have a distinctive profile: nocturnal diastolic hypertension early in the course of OSA.¹⁸ Most patients with untreated OSA do not experience the normal 15 percent to 20 percent fall in blood pressure during nighttime sleep. These "non-dipper" hypertensive patients face an increased risk for stroke or TIA. Untreated systemic hypertension quadruples stroke risk among middle-aged adults with AHI > 15. Developing systemic hypertension triples that risk.^{17,19} Acute ischemic stroke patients who are non-dippers also tend to have more severe strokes and worse stroke outcome.⁴

Undiagnosed OSA should be considered in patients with medically refractory hypertension. One study found 83 percent of undiagnosed OSA non-dippers' hypertension remained uncontrolled despite the use of three or more hypertensive drugs.²⁰

Untreated OSA also is associated with decreased cardiac output, fibrinolytic activity, and cerebral blood flow during apneas; increased platelet aggregability and sympathetic activity; and impaired cerebral blood flow regulation especially during sleep. All of these may predispose patients to stroke

Table 1. Symptoms and signs of adult OSA

- Apneas often end with an arousal, snort, or gasp
- Habitual nightly snoring
- Frequent nighttime awakenings
- Un-refreshing sleep
- Excessive tossing and turning while sleeping
- Dry mouth, nasal congestion, and/or sore throat
- Excessive daytime sleepiness, fatigue, or tiredness
- Depression, irritability, or personality change
- Memory or concentration problems
- Nocturia
- Morning headache

Table 2. Risk factors for OSA

- Male sex (male:female 2-3:1)
- Age (2 to 7 years, middle-aged)
- African-American and Hispanic
- Obesity (BMI > 28 kg/m², especially central pattern)
- Neck circumference > 17 inches in men, > 16.5 inches women
- Waist circumference > 40 inches in men and > 35 inches women
- Habitual snoring (crescendo, gasps, snorts)
- Adenotonsillar hypertrophy
- Unexplained bilateral calf edema
- Craniofacial skeletal abnormalities (especially non-obese children and adults)
- Alcohol, sedative, and/or opiate use
- Hypothyroidism, acromegaly

and TIA.²¹ Untreated OSA also may predispose patients to insulin resistance, diabetes mellitus, and obesity, rather than the other way around.²¹

Diagnosing and treating OSA in acute stroke

With this in mind, I have begun to regularly ask stroke or TIA patients whether they have some or all symptoms and signs of adult OSA. I also confirm the history with a bed partner or family member since OSA patients too often are unaware of their OSA or its effects upon them.^{22,23} (See Table 1.) Be on the alert for OSA in stroke patients who have risk factors for OSA. (See Table 2.)

My hospital has the uncommon luxury of having staff and support to record a comprehensive Type I PSG at the acute stroke patient's bedside. (See Table 3.) If clinicians observe AHI > 15 in the first two hours of recording with the patient sleeping in supine and lateral body positions, typically we introduce and titrate continuous positive airway pressure in the second half of the night through a split-night PSG. Anticipating this, the sleep technologist fits a mask before the study.

Many acute stroke patients do best with full face masks because of difficulty keeping their mouths closed. Heated humidification helps them tolerate CPAP. If the patient shows complex SDB or sleep-related hypoventilation, the clinicians typically repeat the study, testing the efficacy of bilevel positive pressure or even automatic servo-ventilation.

While the Type I PSG effectively diagnoses and treats OSA and SDB in acute stroke patients, we need simpler, cheaper, and less labor-intensive testing methods.

Role of auto-adjusting CPAP

A few studies report effective results using auto-adjusting CPAP devices to diagnose and treat OSA in acute stroke patients.

Researchers validated autoCPAP's use in sleep laboratories by attempting to titrate autoCPAP in all acute stroke patients with AHI > 15 or AHI > 10 who complained of excessive daytime sleepiness.^{2,24,25} Patients willing to use CPAP were discharged home on a fixed CPAP pressure based upon their autoCPAP values. The study recorded Type I PSG and autoCPAP in this subset of patients and found good correlation between AHI. The mean AHI difference between the two was 1.3 with an $r^2 = 0.75$. Another study obtained useable data from autoCPAP studies in 84 percent of acute stroke patients who had OSA.²⁶

However, some researchers reported less success. A study in Valencia, Spain evaluated the effectiveness of using autoCPAP to identify an effective CPAP pressure in hospitalized patients with newly recognized OSA. The researchers encouraged patients to use autoCPAP in hospital, discharged them home on fixed CPAP pressure based on autoCPAP values, and scheduled a follow-up Type I PSG as an outpatient procedure.²⁷ They found autoPAP underestimated the CPAP pressure needed in 60 percent of subjects, and

Table 3. AASM classification of sleep studies

Sleep Study Classification	Description
Type I	Comprehensive attended in-laboratory polysomnography (in-laboratory full PSG, attended by a technologist present during the study)
Type II	Comprehensive unattended portable (unattended, in-laboratory, or at-home but recording all the same physiological parameters typically recorded during an in-laboratory PSG)
Type III	Modified portable unattended sleep apnea testing (limited PSG measuring at least four cardiorespiratory parameters done either at home or in laboratory without a technologist present)
Type IV	Continuous single or dual bioparameter unattended testing (very limited PSG recording; only one to two cardiorespiratory parameters typically recorded unattended at home)

*Table modified from a table by Ferber R, Millman R, Coppola M, Fleetham J, Murray CF, Iber C, et al. Portable recording in the assessment of obstructive sleep apnea. *ASDA standards of practice. Sleep.* 1994;17(4):378-92.³⁴

21 percent required bilevel PAP for optimal control of their SDB.²⁷

Alternative screening methods

Researchers have tried screening for OSA in acute stroke patients using simplified sleep apnea monitoring devices which only record airflow, respiratory effort, oxygen saturation, and heart rate or EKG, but provide no information as to sleep/wake state or body position.⁴⁹ The AASM classifies these devices as Type III tests. (See Table 3.)

Because Type III devices and studies report AHI as time in bed, the AHI may be falsely low if the

patient lies awake much of the night. A recent assessment of Type III studies and devices indicated they might lessen the expense and time to diagnosis compared with a Type I PSG because often they cost half the price of a Type I PSG. However, unusable data remain a problem.²⁸

Clinicians using nocturnal pulse oximetry to screen for OSA in stroke rehabilitation patients have met other obstacles.¹¹ The classic oximetry pattern seen in patients with OSA includes repetitive drops in oxygen saturation of 2 percent to 4 percent or greater, which usually last less than 60 seconds followed by recovery to 90 percent or greater. Some patients with OSA will show a fall in their baseline oxygen saturation to less than 90 percent during REM sleep, when sleeping supine, or secondary to sensor recording problems.

Nocturnal pulse oximetry has poor sensitivity and specificity for diagnosing or confirming OSA. The test can identify OSA if positive but cannot exclude OSA if results are negative.

It usually will identify most patients with moderate to severe OSA, but often it records false-negative in patients with milder forms of OSA whose respiratory events cause little or no oxygen desaturation.

Finally, abnormal oximetry results are not OSA-specific and often are seen in patients with lung disease.

Researchers at the University Hospital of Munster, Germany studied whether they could diagnose OSA in acute stroke patients by using trend graphs in end-tidal carbon dioxide values.²⁹ They scored AHI events when the ET_{CO₂} dropped below 50 percent of the previous baseline value. The study found a mean of five ET_{CO₂} drops per hour were highly predictive that an AHI of > 10 would be recorded using a Type III device.²⁹

Long-term CPAP compliance

Clinicians have few guidelines for determining which patients need CPAP. The Spanish Society of Pneumology and Thoracic Surgery recommended CPAP for all patients with an AHI > 30, even those who claimed themselves asymptomatic, and those with AHI 5 to 30 who reported EDS or had polycythemia or heart failure.³⁰

Researchers have found success titrating CPAP in 69 percent of acute stroke patients with SDB who had AHI > 15 or AHI > 10 with EDS; more than half of patients were discharged home on fixed-rate CPAP. Only 72 percent of these patients

returned in follow-up, and 31 percent who needed it were still using the CPAP. Just 15 percent of patients with OSA during the acute stroke period used CPAP long term. Improvement in SDB occurred in most patients, with normalization of the AHI in 40 percent of patients.³¹

However, long-term compliance with CPAP in patients with OSA who have had a stroke or TIA remains poor.^{2,7,32} Aphasia and severity of motor deficits were predictors of poor CPAP compliance in patients with stroke.³¹

Clinicians need to emphasize CPAP's benefits to OSA patients, in order to improve adherence to therapy. These include the following:

- preventing or improving hypertension
- reducing abnormal elevations of inflammatory cytokines and adhesion molecules
- reducing excessive sympathetic tone
- helping avoid increased vascular oxidative stress
- reversing coagulation abnormalities
- reducing leptin levels
- reducing the development of fatty liver
- reducing recurrent stroke
- improving control of diabetes mellitus and hypertension.²¹

Cost-effectiveness of screening and treatment

Screening and treating OSA in stroke patients can be cost-effective.³³ Researchers from the University of Michigan compared two alternative strategies: PSG followed by three months of CPAP for those who had OSA vs. no screening.

They found the screening resulted in an incremental cost savings of \$49,421 per quality adjusted life-year and determined it appeared cost-effective. However, researchers theorized a split-night PSG protocol titrating CPAP in the second half of the study might yield further savings.

For a list of references, look under the "Magazine" tab at www.advanceweb.com/respmanager. ■

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