HHS Public Access

Author manuscript

Sleep Health. Author manuscript; available in PMC 2018 March 03.

Published in final edited form as:

Sleep Health. 2015 December ; 1(4): 244–248. doi:10.1016/j.sleh.2015.09.005.

Obstructive sleep apnea and stroke: links to health disparities[☆, ☆☆]

Alberto R. Ramos, MD, MSPH[a,b,*], **Azizi Seixas, PhD**[c], and **Salim I. Dib, MD**[a,b]

[a]Department of Neurology, University of Miami, Miller School of Medicine, Miami, FL

[b]Sleep Disorders Program, Bascom Palmer Eye Institute, University of Miami, Miller School of Medicine, Miami, FL

[c]Center for Healthful Behavior Change, Department of Population Health, New York University, School of Medicine, New York, NY

Abstract

Obstructive sleep apnea (OSA) is a novel cardiovascular and cerebrovascular risk factor that presents unique opportunities to understand and reduce seemingly intractable stroke disparity among non-Hispanic blacks and Hispanic/Latinos. Individuals from these 2 groups have up to a 2-fold risk of stroke and greater burden of OSA. Obstructive sleep apnea directly and indirectly increases risk of stroke through a variety of autonomic, chemical, and inflammatory mechanisms and vascular risk factors such as hypertension, obesity, and diabetes mellitus. Untreated OSA exacerbates poststroke prognosis, as it may also influence rehabilitation efforts and functional outcomes such as cognitive function after a stroke. Conversely, treatment of OSA may reduce the risk of stroke and may yield better poststroke prognosis. Unfortunately, in racial/ethnic minority groups, there are limited awareness, knowledge, and screening opportunities for OSA. Increasing awareness and improving screening strategies for OSA in minorities may alleviate stroke risk burden and improve stroke outcomes in these populations. This review article is intended to highlight the epidemiology, clinical characteristics, pathophysiology, diagnosis, and treatment of OSA in relation to stroke risk, with an emphasis on race-ethnic disparities.

Keywords

Obstructive sleep apnea; Stroke; Sleep duration; Vascular cognitive impairment; Health disparities; Black; Hispanics/Latinos

☆Funding: The project described was also supported by grant number 1KL2TR000461 (ARR), Miami Clinical and Translational Science Institute, from the National Center for Advancing Translational Sciences and the National Institute on Minority Health and Health Disparities. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.

☆☆Diversity supplement to the National Institute of Neurological Disorders and Stroke of the National Institutes of Health under grant number U54NS081765 (AAS).

*Corresponding author at: UHealth Sleep Medicine Program, Assistant Professor of Neurology, University of Miami Miller School of Medicine, Miami, FL. Tel.: +1 305 243 8393, +1 305 243 9999 (Sleep Center); fax: +1 305 243 5403. aramos@med.miami.edu (A.R. Ramos).

Disclosures

The authors do not have anything to disclose.

Introduction

Stroke remains one of the leading causes of death in the United States. There are approximately 795,000 annual cases and 130,000 stroke related deaths in the United States, making it the fifth leading cause of death. However, stroke remains the second leading cause of adult death worldwide and the leading cause of adult disability.[1,2]

Racial/ethnic minorities, such as non-Hispanic blacks (herein referred to as blacks) and US Hispanics, compared to non-Hispanic whites carry a large burden of the disease.[3,4] Although the burden of stoke is well-documented among blacks, US Hispanic stroke rates are less well documented. Available studies suggest that US Hispanics have over a 2-fold increased stroke risk compared to non-Hispanic whites.[5,6] Treatment of vascular risk factors, such as hypertension, tobacco, and diabetes mellitus, improved the prevention and stroke outcomes.[7] However, the presence of these vascular risk factors explains about half of the strokes, particularly among minority populations. Therefore, it is imperative to focus on novel risk factors for stroke.[8,9]

Obstructive sleep apnea (OSA) is a novel risk factor for stroke and cardiovascular mortality. Long-term follow-up of the Sleep Heart Health Study and the Wisconsin Sleep Cohort shows nearly 3- to 4-fold higher associations between baseline OSA and incident stroke.[10–12]

The Sleep Heart Health Study observed an increased risk of stroke in men with moderate to severe OSA (hazard ratio of 2.9; 95% confidence interval [CI], 1.1–7.4), whereas women with an apnea-hypopnea index (AHI) of 25 or more also had an increased stroke risk after a median of 8.7 years.[13] However, sparse data are available describing sleep and stroke risk in minorities.

Mounting evidence suggests that OSA is also related to subclinical brain infarcts and ischemic white matter hyperintensities by magnetic resonance imaging, markers of cerebral small vessel disease, which predict incident stroke and vascular cognitive impairment.[14–16]

This review article summarizes the relationship between OSA and stroke, with specific emphasis on health disparities among US non-Hispanic blacks and Hispanics/Latinos. We review the association of OSA with vascular risk factors and the mechanisms that may lead to increased stroke risk in OSA. In addition, we discuss the association between intermediate phenotypes associated with stroke, such as subclinical markers of cerebrovascular disease and vascular cognitive impairment.

Prevalence and risk factors for OSA in race-ethnic minorities

Obstructive sleep apnea is characterized by loud and frequent snoring, witnessed apneas, excessive daytime sleepiness, fatigue, poor concentration, restlessness, and morning headaches. The diagnosis of OSA is confirmed by polysomnography or home-sleep testing. Factors such as being male, increased body mass index ≥30, and hypertension are associated with an increased likelihood of OSA.[16]

Some estimate that the prevalence of OSA in the United States is approximately 17% in adults and, of these, up to 25% are older than 65 years. However, the prevalence could be higher in minorities as few population-based studies indicate that a significant amount of racial/ethnic minorities report OSA-like symptoms.[17,18] In a sample of community-dwelling blacks from the Jackson Heart Study, snoring was reported by 66.3% of men and 58% of women, whereas daytime sleepiness was reported by 68.6% of men and 61.4% of women.[19] The Cleveland Family Study, using polysomnography to confirm OSA, found a higher frequency of OSA among blacks (31%) compared to whites (10%).[20] A meta-analysis of 10 studies showed an increased frequency and severity of sleep apnea among blacks compared to non-Hispanic whites.[21] In addition, in The Hispanic Community Health Study/Study of Latinos (HCHS/SOL), the largest study of Hispanic/Latinos in the United States, 34% of men and 18% of women met criteria for OSA, using the minimal criteria of an AHI ≥5.[22] Some estimates suggest that up to 93% of women and 82% of men with moderate to severe OSA remain untreated.[16]

Because blacks and Hispanics have an increased risk of medical conditions that are related to OSA, it is likely that the prevalence of OSA may be greater. Blacks and Hispanic/Latinos compared to whites have higher obesity, hypertension, and cardiometabolic abnormalities (metabolic syndrome and diabetes mellitus) frequencies, which should prompt physicians to evaluate and risk-stratify for OSA among these groups.[23–25] In a cross-sectional analysis of 280 patients with OSA, blacks were more likely to be obese and hypertensive, compared to non-Hispanic whites,[26] whereas participants with moderate to severe OSA (AHI ≥15) from HCHS/SOL had a 90% higher chance of diabetes mellitus and 44% higher chance of hypertension.[22]

There are risk prediction tools, such as the Berlin, the STOP-BANG, and the ARES questionnaire, used in clinical samples and community-based populations that risk-stratify the likelihood of OSA,[27–29] before polysomnography. Although these risk prediction tools are helpful, there are little data in poststroke populations and minorities. Of these, the Berlin questionnaire had moderate diagnostic utility in stroke patients, with a sensitivity of 60% to 70% and specificity of 15% to 55%.[13,30] Despite these high rates and considerable progress in diagnostic tools, most racial/ethnic minorities with OSA remain undiagnosed.

Several studies used OSA predicting tools in stroke and minorities with mixed results. For example, in patients with acute strokes admitted to a tertiary stroke center, Hispanic/Latinos (mostly from Cuban descent) had a higher risk of sleep apnea (based on the Berlin questionnaire) than either black or white participants.[31] These findings were not reproduced by the Brain Attack Surveillance in Corpus Christi sleep apnea study, where prestroke sleep apnea risk did not differ between Hispanic/Latinos of Mexican descent and white participants,[32] but further studies are needed in other Hispanic groups and black patients.

Vascular mechanisms between OSA and stroke

Obstructive sleep apnea may causally lead to stroke through its associations with potent vascular risk factors, such as hypertension, diabetes mellitus, obesity, and atrial fibrillation. Of aforementioned factors, hypertension is considered the strongest predictor and the main

modifiable risk factor for stroke. Sleep apnea is independently associated with hypertension and increases the risk of hypertension in a dose-response pattern. Mild OSA, AHI of 5 to 14, was associated with a 2-fold risk of hypertension, whereas those with moderate to severe OSA (AHI ≥15) had a 3-fold risk at 4 years of follow-up. Obesity is a known risk factor for OSA and has been associated with a host of inflammatory and metabolic abnormalities that promote insulin resistance.[25,33] Conversely, physiological perturbations associated with intermittent hypoxemia and increased sympathetic tone also increase risk of obesity and diabetes mellitus in OSA.[34,35] Obstructive sleep apnea leads to altered levels of leptin, a hormone secreted by adipocytes, which promotes the sensation of satiety and increases the metabolic rate. Untreated OSA causes resistance to the metabolic effects of leptin, promoting weight gain and obesity.

Obstructive sleep apnea is associated with a host of cardiac arrhythmias, but relevant to stroke risk is the association between OSA and atrial fibrillation (AF).[36–38] Patients with severe sleep apnea have a 4-fold increased risk of AF, an established risk factor for cardioembolic strokes.[36] Some suggest that OSA may trigger AF by stretching the atrial chamber secondary to swings in the intrathoracic pressure, increasing the left ventricular end-diastolic pressure and possibly increased systemic inflammation. It is hypothesized that vascular strain may lead to cardiac remodeling, which contribute to AF.[36–38]

Obstructive sleep apnea may also promote cerebrovascular disease through increased sympathetic tone, reduction in cerebral blood flow, altered cerebral autoregulation, impaired endothelial function, increased platelet activation, inflammation, and oxidative stress related to the intermittent hypoxemia-reoxygenation.[39] Obstructive sleep apnea can lead to reductions in cerebral blood flow and impaired cerebral autoregulation, possibly damaging the small vessels in the brain.

Few cross-sectional studies show associations between OSA and large vessel subclinical atherosclerosis, such as increased carotid intima-media thickness and carotid plaques, with vibratory trauma from loud snoring potentially playing a role of carotid endothelial function.[40–42] Hypoxemia and reoxygenation leads to oxidant-mediated endothelial dysfunction, which contributes to the athero-sclerotic process and may be reversed by treatment with continuous positive airway pressure.[21,43,44]

Treatment of OSA in stroke

Initial treatment of OSA includes avoiding or minimizing factors that may exacerbate OSA (ie, benzodiazepines). Continuous positive airway pressure (CPAP) is the first-line therapy for patients with moderate to severe OSA. Aside from improving sleep quality and daytime symptoms (ie, sleepiness), CPAP could decrease cardiovascular events and has modest effects on blood pressure. Interestingly, in a 5-year prospective observational study of patients with OSA and stroke, individuals with moderate or severe OSA who were nonadherent to CPAP had increased risk of cardiovascular disease or stroke mortality (hazard ratio, 1.6; 95% CI, 1.0–2.5), compared to those adherent to CPAP.[8,40] However, data on OSA and stroke-specific outcomes are limited. An observational study of 96 patients with ischemic strokes and OSA treated if the AHI was ≥20 showed lower mortality at 5 years and

fewer nonfatal cardiovascular events at 7 years among patients who complied with CPAP compared to those who did not.[45,46]

Sleep and vascular cognitive impairment

Cognitive impairment is 1 functional area that is often affected by comorbid OSA and stroke. Vascular cognitive impairment is caused by or associated with stroke and subclinical cerebrovascular disease,[47] which may lead to dementia.[40] The relationship between OSA and cognitive impairment among minorities is of particular concern, as some estimate increased risk of dementia in these populations.[48] It is plausible that OSA and its association with stroke and cerebrovascular disease contribute to vascular cognitive impairment. There is overwhelming evidence that individuals with OSA show a wide variety of neurocognitive impairments, in the following areas: attention, constructional abilities, executive functioning, language abilities, memory, psychomotor speed, and visuospatial abilities.[49–51]

In the Osteoporotic Fractures Study, elderly women (mean age of 82 years) with and without OSA were followed for a median of 5 years. Compared to the 193 women without OSA, the 105 women (35.2%) with moderate to severe OSA (AHI >15 events per hour of sleep) had a greater odds of cognitive impairment and dementia (31.1% vs 44.8%) in multivariable analysis (adjusted odds ratio = 1.85; 95% CI, 1.11–3.08).[51] In addition, daytime sleepiness predicted vascular dementia, but not nonvascular dementia, in a large community-based cohort of older men.[52]

The field is undecided about a clear etiology of OSA-related cognitive impairment, as some espouse that OSA is characterized by and accompanied with sleep fragmentation, daytime sleepiness, and nocturnal hypoxemia, which, in turn, induces a host of cognitive impairments. One established etiological framework suggests that cognitive impairment is caused by frequent sleep disruptions, particularly as a result of hypoxemia. Several studies indicate that cognitive impairment is worsened by the presence of key comorbidities such as cardiovascular disease, obesity, and physical inactivity. However, little has been done to investigate the effect nonmedical factors, such as race and sex, have on the association among OSA, stroke, and neurocognitive impairment. However, there appears to be initial evidence that sex and race contribute to the OSA–cognitive impairment relationship. In a study of 88 patients with OSA, race and sex impacted OSA-related cognitive impairment, which led to poor CPAP adherence.[53] However, these studies only provide assessments of crude neurocognitive function and OSA symptoms and lack specificity about how certain OSA symptoms induce certain neurocognitive impairments, among racial and ethnic minority groups. For example, the aforementioned study used the Mail-In Cognitive Function Screening Instrument, a self-report screening tool, to assess cognitive impairment, which has significant limitations in distinguishing specific cognitive domains.[53]

Recent data from HCHS/SOL evaluated the associations between OSA and cognitive function in more than 8000 Hispanics/Latinos from 4 urban areas. In this cross-sectional analysis, OSA was associated with worse cognitive function among women, compared to men, in the domains of memory, language, and executive function. The association was stronger in younger (45–54 years) than older women (65–74 years).[54] However, more

studies are needed to evaluate the effects race/ethnicity and sex has on cognitive impairment among individuals with OSA and stroke.

Sleep duration, sleep apnea, and stroke

Short sleep (<5–6 hours) and long sleep (>8–9 hours) durations are associated with stroke and overall increased mortality. Recent findings from the European Prospective Investigation of Cancer study with 9692 participants showed more than a 3-fold stroke risk in participants that changed their sleep duration from short to long sleep up to 4 years after baseline.[55,56] A systematic review and meta-analysis of longitudinal population studies showed both short and long sleep durations to be associated with the incidence of stroke, with stronger associations for long sleep. In addition, a recent longitudinal analysis of the National Health Interview Survey 2004–2013 observed an increased risk of stroke among participants with long sleep duration (odds ratio = 1.43; 95% CI, 1.32–1.52) accounting for 34 demographic, medical, behavioral, and psychosocial factors.[57] Short sleep is associated with obesity, diabetes, hypertension, and the metabolic syndrome, which may lead to increases in stroke risk.[58,59] In cross-sectional studies, long sleep duration was associated with carotid artery atherosclerosis, left ventricular mass, and increased cerebral white matter hyperintensities. However, there is a paucity of mechanisms that explain the relation between long sleep and stroke.[14,60,61] Some suggest that the association between long sleep duration and the incidence of stroke may be better explained by unmeasured confounders such as OSA.[60]

Similar to OSA, there are race-ethnic differences in sleep duration, with blacks consistently reporting shorter and longer sleep durations, relative to non-Hispanic whites.[25] There is some variability in the frequency of short and long sleep duration across Hispanic/Latinos subgroups, with Mexicans reporting average (7–8 hours) to longer hours of sleep and other Hispanic/Latino subgroups reporting increased frequency of short sleep.[62] Although a multitude of studies show strong associations between sleep duration and adverse health outcomes, the majority do not account for the confounding effects of OSA. This is particularly relevant in long sleep duration, which is also associated with OSA, and may explain, mediate, or be a harbinger of stroke.

Summary and future directions

There is a paucity of studies evaluating the specific contribution of OSA and stroke risk among blacks and Hispanic/Latinos, who have up to a 2-fold risk of stroke, increased frequency of sleep symptoms, and OSA. Therefore, it is important to determine the specific ethnic-related stroke risk and the potential barriers to identifying and treating OSA among these populations. Future studies should disentangle short and long sleep duration from OSA and evaluate their independent contribution to stroke risk among minorities. There are limited awareness, knowledge, and screening opportunities for OSA among minorities at risk for stroke. Improving these opportunities may be especially advantageous to minorities in reducing disparities. For example, an ongoing randomized controlled trial of a culturally-tailored, telephone-delivered behavioral intervention to improve the adherence to CPAP in blacks with OSA and metabolic syndrome may serve as a framework by which future clinical studies use patient-centered and culturally-tailored treatments in OSA and stroke.[63]

Randomized clinical trials are needed to determine whether treatments for OSA are effective in the primary prevention of stroke and other cerebrovascular phenotypes, such as vascular cognitive impairment. In addition, the benefits and timing of CPAP therapy after an acute stroke are not established. However, OSA patients at increased stroke risk or those who had a stroke should be risk-stratified, evaluated, and encouraged to use CPAP regularly as part of standard stroke care,[39] and because blacks and Hispanics have a history of poor CPAP compliance, culturally-tailored interventions are needed to increase CPAP compliance to reduce stroke events.[64]

Notably, there is a paucity of tested psychosocial mechanistic pathways to explain the differences across ethnicity/race groups and sleep.[65] Answering this question has the potential to inform our understandings of: (1) discrepancies in OSA-related morbidity and OSA-related comorbid medical conditions, potentially modifying the stroke risk and cerebrovascular burden in these populations; and (2) CPAP adherence and OSA-related quality of life in minorities.

References

1. Go AS, Mozaffarian D, Roger VL, et al. Executive summary: heart disease and stroke statistics—2014 update: a report from the American Heart Association. Circulation. 2014; 129(3):399–410. [PubMed: 24446411]
2. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. Circulation. 2014; 129(3):e28–292. [PubMed: 24352519]
3. Kleindorfer DO, Khoury J, Moomaw CJ, et al. Stroke incidence is decreasing in whites but not in blacks: a population-based estimate of temporal trends in stroke incidence from the Greater Cincinnati/Northern Kentucky Stroke Study. Stroke. 2010; 41(7):1326–1331. [PubMed: 20489177]
4. Kissela BM, Khoury JC, Alwell K, et al. Age at stroke: temporal trends in stroke incidence in a large, biracial population. Neurology. 2012; 79(17):1781–1787. [PubMed: 23054237]
5. Morgenstern LB, Smith MA, Sanchez BN, et al. Persistent ischemic stroke disparities despite declining incidence in Mexican Americans. Ann Neurol. 2013; 74(6):778–785. [PubMed: 23868398]
6. Sacco RL, Boden-Albala B, Abel G, et al. Race-ethnic disparities in the impact of stroke risk factors: the northern Manhattan stroke study. Stroke. 2001; 32(8):1725–1731. [PubMed: 11486097]
7. Goldstein LB, Bushnell CD, Adams RJ, et al. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011; 42(2):517–584. [PubMed: 21127304]
8. Diaz J, Sempere AP. Cerebral ischemia: new risk factors. Cerebrovasc Dis. 2004; 17(Suppl 1):43–50. [PubMed: 14694279]
9. Howard G, Cushman M, Kissela BM, et al. Traditional risk factors as the underlying cause of racial disparities in stroke: lessons from the half-full (empty?) glass. Stroke. 2011; 42(12):3369–3375. [PubMed: 21960581]
10. Arzt M, Young T, Finn L, Skatrud JB, Bradley TD. Association of sleep-disordered breathing and the occurrence of stroke. Am J Respir Crit Care Med. 2005; 172(11):1447–1451. [PubMed: 16141444]
11. Redline S, Yenokyan G, Gottlieb DJ, et al. Obstructive sleep apnea-hypopnea and incident stroke: the sleep heart health study. Am J Respir Crit Care Med. 2010; 182(2):269–277. [PubMed: 20339144]
12. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. N Engl J Med. 2005; 353(19):2034–2041. [PubMed: 16282178]

13. Srijithesh PR, Shukla G, Srivastav A, Goyal V, Singh S, Behari M. Validity of the Berlin Questionnaire in identifying obstructive sleep apnea syndrome when administered to the informants of stroke patients. J Clin Neurosci. 2011; 18(3):340–343. [PubMed: 21237648]
14. Ramos AR, Dong C, Rundek T, et al. Sleep duration is associated with white matter hyperintensity volume in older adults: the Northern Manhattan Study. J Sleep Res. 2014; 23(5):524–530. [PubMed: 25040435]
15. Wright CB, Festa JR, Paik MC, et al. White matter hyperintensities and subclinical infarction: associations with psychomotor speed and cognitive flexibility. Stroke. 2008; 39(3):800–805. [PubMed: 18258844]
16. Wallace DM, Ramos AR, Rundek T. Sleep disorders and stroke. Int J Stroke. 2012; 7(3):231–242. [PubMed: 22336145]
17. O'Connor GT, Lind BK, Lee ET, et al. Variation in symptoms of sleep-disordered breathing with race and ethnicity: the Sleep Heart Health Study. Sleep. 2003; 26(1):74–79. [PubMed: 12627736]
18. Ramos AR, Wohlgemuth WK, Dong C, et al. Race-ethnic differences of sleep symptoms in an elderly multi-ethnic cohort: the Northern Manhattan Study. Neuroepidemiology. 2011; 37(3–4): 210–215. [PubMed: 22123526]
19. Fulop T, Hickson DA, Wyatt SB, et al. Sleep-disordered breathing symptoms among African-Americans in the Jackson Heart Study. Sleep Med. 2012; 13(8):1039–1049. [PubMed: 22841028]
20. Redline S, Tishler PV, Hans MG, Tosteson TD, Strohl KP, Spry K. Racial differences in sleep-disordered breathing in African-Americans and Caucasians. Am J Respir Crit Care Med. 1997; 155(1):186–192. [PubMed: 9001310]
21. Ruiter ME, DeCoster J, Jacobs L, Lichstein KL. Sleep disorders in African Americans and Caucasian Americans: a meta-analysis. Behav Sleep Med. 2010; 8(4):246–259. [PubMed: 20924837]
22. Redline S, Sotres-Alvarez D, Loredo J, et al. Sleep-disordered Breathing in Hispanic/Latino Individuals of Diverse Backgrounds. The Hispanic Community Health Study/Study of Latinos. Am J Respir Crit Care Med. 2014; 189(3):335–344. [PubMed: 24392863]
23. Olafiranye O, Akinboboye O, Mitchell JE, Ogedegbe G, Jean-Louis G. Obstructive sleep apnea and cardiovascular disease in blacks: a call to action from the Association of Black Cardiologists. Am Heart J. 2013; 165(4):468–476. [PubMed: 23537962]
24. Pandey A, Williams N, Donat M, et al. Linking sleep to hypertension: greater risk for blacks. Int J Hypertens. 2013; 2013:436502. [PubMed: 23710339]
25. Adenekan B, Pandey A, McKenzie S, Zizi F, Casimir GJ, Jean-Louis G. Sleep in America: role of racial/ethnic differences. Sleep Med Rev. 2013; 17(4):255–262. [PubMed: 23348004]
26. Meetze K, Gillespie MB, Lee FS. Obstructive sleep apnea: a comparison of black and white subjects. Laryngoscope. 2002; 112(7 Pt 1):1271–1274. [PubMed: 12169912]
27. Coelho FM, Pradella-Hallinan M, Palombini L, Tufik S, Bittencourt LR. The STOP-BANG questionnaire was a useful tool to identify OSA during epidemiological study in Sao Paulo (Brazil). Sleep Med. 2012; 13(4):450–451.
28. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999; 131(7):485–491. [PubMed: 10507956]
29. Enciso R, Clark GT. Comparing the Berlin and the ARES questionnaire to identify patients with obstructive sleep apnea in a dental setting. Sleep Breath. 2011; 15(1):83–89. [PubMed: 20127186]
30. Kepplinger J, Barlinn K, Albright KC, et al. Early sleep apnea screening on a stroke unit is feasible in patients with acute cerebral ischemia. J Neurol. 2013; 260(5):1343–1350. [PubMed: 23263538]
31. Ramos AR, Guilliam D, Dib SI, Koch S. Race/ethnic differences in obstructive sleep apnea risk in patients with acute ischemic strokes in south Florida. Sleep Breath. 2014; 18(1):165–168. [PubMed: 23771345]
32. De Lott LB, Lisabeth LD, Sanchez BN, et al. Prevalence of pre-stroke sleep apnea risk and short or long sleep duration in a bi-ethnic stroke population. Sleep Med. 2014; 15(12):1582–1585. [PubMed: 25454982]
33. de Mello MT, Narciso FV, Tufik S, et al. Sleep disorders as a cause of motor vehicle collisions. Int J Prev Med. 2013; 4(3):246–257. [PubMed: 23626880]

34. Barone MT, Menna-Barreto L. Diabetes and sleep: a complex cause-and-effect relationship. Diabetes Res Clin Pract. 2011; 91(2):129–137. [PubMed: 20810183]
35. Pandey A, Demede M, Zizi F, et al. Sleep apnea and diabetes: insights into the emerging epidemic. Curr Diab Rep. 2011; 11(1):35–40. [PubMed: 21069483]
36. Malhotra A, Neilan TG, Sarmiento K. Obstructive sleep apnea and atrial fibrillation: is the link real? J Am Coll Cardiol. 2014; 64(19):2024–2025. [PubMed: 25440098]
37. Shah RV, Abbasi SA, Heydari B, et al. Obesity and sleep apnea are independently associated with adverse left ventricular remodeling and clinical outcome in patients with atrial fibrillation and preserved ventricular function. Am Heart J. 2014; 167(4):620–626. [PubMed: 24655713]
38. Neilan TG, Farhad H, Dodson JA, et al. Effect of sleep apnea and continuous positive airway pressure on cardiac structure and recurrence of atrial fibrillation. J Am Heart Assoc. 2013; 2(6):e000421. [PubMed: 24275628]
39. Culebras A. Sleep apnea and stroke. Curr Neurol Neurosci Rep. 2015; 15(1):503. [PubMed: 25407131]
40. Ramos A, Dib S, Wright C. Vascular dementia. Curr Transl Geriatr Exp Gerontol Rep. 2013; 2(3): 188–195. [PubMed: 26213642]
41. Placidi F, Diomedi M, Cupini LM, Bernardi G, Silvestrini M. Impairment of daytime cerebrovascular reactivity in patients with obstructive sleep apnoea syndrome. J Sleep Res. 1998; 7(4):288–292. [PubMed: 9844856]
42. Virtanen J, Noponen T, Salmi T, Toppila J, Merilainen P. Impaired cerebral vasoreactivity may cause cerebral blood volume dip following obstructive sleep apnea termination. Sleep Breath. 2012; 16(2):309–312. [PubMed: 21553349]
43. Jelic S, Padeletti M, Kawut SM, et al. Inflammation, oxidative stress, and repair capacity of the vascular endothelium in obstructive sleep apnea. Circulation. 2008; 117(17):2270–2278. [PubMed: 18413499]
44. Kohler M, Craig S, Nicoll D, Leeson P, Davies RJ, Stradling JR. Endothelial function and arterial stiffness in minimally symptomatic obstructive sleep apnea. Am J Respir Crit Care Med. 2008; 178(9):984–988. [PubMed: 18658111]
45. Martinez-Garcia MA, Campos-Rodriguez F, Soler-Cataluna JJ, Catalan-Serra P, Roman-Sanchez P, Montserrat JM. Increased incidence of nonfatal cardiovascular events in stroke patients with sleep apnoea: effect of CPAP treatment. Eur Respir J. 2012; 39(4):906–912. [PubMed: 21965227]
46. Martinez-Garcia MA, Soler-Cataluna JJ, Ejarque-Martinez L, et al. Continuous positive airway pressure treatment reduces mortality in patients with ischemic stroke and obstructive sleep apnea: a 5-year follow-up study. Am J Respir Crit Care Med. 2009; 180(1):36–41. [PubMed: 19406983]
47. Gorelick PB, Pantoni L. Advances in vascular cognitive impairment. Stroke. 2013; 44(2):307–308. [PubMed: 23321448]
48. 2010 Alzheimer's disease facts and figures. Alzheimers Dement. 2010; 6(2):158–194. [PubMed: 20298981]
49. Andreou G, Agapitou P. Reduced language abilities in adolescents who snore. Arch Clin Neuropsychol. 2007; 22(2):225–229. [PubMed: 17293079]
50. Cohen-Zion M, Stepnowsky C, Marler Shochat T, Kripke DF, Ancoli-Israel S. Changes in cognitive function associated with sleep disordered breathing in older people. J Am Geriatr Soc. 2001; 49(12):1622–1627. [PubMed: 11843994]
51. Yaffe K, Laffan AM, Harrison SL, et al. Sleep-disordered breathing, hypoxia, and risk of mild cognitive impairment and dementia in older women. JAMA. 2011; 306(6):613–619. [PubMed: 21828324]
52. Elwood PC, Bayer AJ, Fish M, Pickering J, Mitchell C, Gallacher JE. Sleep disturbance and daytime sleepiness predict vascular dementia. J Epidemiol Community Health. 2011; 65(9):820–824. [PubMed: 20675705]
53. Bade BC, Strange C, Lal C. Effect of obstructive sleep apnea treatment on mail-in cognitive function screening instrument. Am J Med Sci. 2014; 348(3):215–218. [PubMed: 24736766]
54. Ramos AR, Tarraf W, Rundek T, et al. Obstructive sleep apnea and neurocognitive function in a Hispanic/Latino population. Neurology. 2015; 84(4):391–398. [PubMed: 25540308]

55. Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J. 2011; 32(12):1484–1492. [PubMed: 21300732]

56. Leng Y, Cappuccio FP, Wainwright NW, et al. Sleep duration and risk of fatal and nonfatal stroke: a prospective study and meta-analysis. Neurology. 2015; 84(11):1072–1079. [PubMed: 25716357]

57. Seixas AA, Gyamfi L, Atiase Y, Gordon G, Zizi F, Jean-Louis G. Long, rather than short sleep, is a predictor of stroke risk: a comparative analysis of multiple linear regression model and Bayesian belief network model. Sleep. 2015; 38:A293. abstract supplement.

58. Gangwisch JE, Heymsfield SB, Boden-Albala B, et al. Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey. Hypertension. 2006; 47(5):833–839. [PubMed: 16585410]

59. Gottlieb DG, Punjabi NM, Newman AB, et al. Short sleep time is associated with diabetes mellitus and impaired glucose tolerance. Arch Intern Med. 2005; 165(8):863–867. [PubMed: 15851636]

60. Grandner MA, Drummond SP. Who are the long sleepers? Towards an understanding of the mortality relationship. Sleep Med Rev. 2007; 11(5):341–360. [PubMed: 17625932]

61. Ramos AR, Jin Z, Rundek T, et al. Relation between long sleep and left ventricular mass (from a multiethnic elderly cohort). Am J Cardiol. 2013; 111:599–603.

62. Loredo JS, Soler X, Bardwell W, Ancoli-Israel S, Dimsdale JE, Palinkas LA. Sleep health in U.S. Hispanic population. Sleep. 2010; 33(7):962–967. [PubMed: 20614856]

63. Williams NJ, Jean-Louis G, Brown CD, McFarlane SI, Boutin-Foster C, Ogedegbe G. Telephone-delivered behavioral intervention among blacks with sleep apnea and metabolic syndrome: study protocol for a randomized controlled trial. Trials. 2014; 15:225. [PubMed: 24925227]

64. Wallace DM, Wohlgemuth WK. Does race-ethnicity moderate the relationship between CPAP adherence and functional outcomes of sleep in US veterans with obstructive sleep apnea syndrome? J Clin Sleep Med. 2014; 10(10):1083–1091. [PubMed: 25317089]

65. Petrov, ME., Lichstein, KL. Differences in sleep between black and white adults: an update and future directions. Sleep Med. 2015. http://dx.doi.org/10.1016/j.sleep.2015.01.011 [pii: S1389-9457(15)00057-X, Epub ahead of print, in press]