



OBSTRUCTIVE SLEEP APNEA AS AN INDEPENDENT STROKE RISK FACTOR: A REVIEW OF THE EVIDENCE, STROKE PREVENTION GUIDELINES, AND IMPLICATIONS FOR NEUROSCIENCE NURSING PRACTICE

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ABSTRACT

Stroke is a leading cause of death and disability affecting nearly 800,000 people in the United States every year. Obstructive sleep apnea (OSA) is found in over 60% of patients with stroke/transient ischemic attack (TIA) and identified as an independent stroke risk factor in large epidemiology studies and Canadian Stroke Prevention Guidelines (SPG) but not in the United States. The 2014 Secondary SPG recommend OSA screening and treatment as a consideration only, not a requirement. The twofold purpose of this article is, first, to present the evidence supporting OSA as an independent stroke risk factor in national SPG with mandatory recommendations and, second, to engage neuroscience nurses to incorporate OSA assessment and interventions into the nursing process and thereby promote excellence in stroke/TIA patient care. Methods: A systematic literature search was conducted in Medline, CINAHL, and PubMed to identify research from 2003 through 2013 on the independent risk, mortality, and prevalence relationship between OSA and stroke/TIA including recurrence and recovery outcomes with continuous positive airway pressure (CPAP) therapy. Results: Twenty-eight research articles were reviewed: 14 observational cohorts, five case-control studies, four cross-sectional studies, and four randomized control trials representing 12 countries and 10,671 subjects. Discussion: OSA is highly prevalent in patients with stroke/TIA independently increasing stroke risk. CPAP studies revealed reduced stroke recurrence and improved recovery with feasible initiation in stroke units. Patients with stroke/TIA have less OSA-associated daytime sleepiness and obesity, making the usual screening tools insufficient and CPAP adherence challenging. Treating OSA decreases stroke prevalence and mortality. OSA initiatives empower neuroscience nurses to integrate this OSA evidence into clinical practice and improve stroke/TIA patient outcomes.

Keywords : **obstructive sleep apnea, sleep-disordered breathing, stroke risk**

INTRODUCTION

In the United States, stroke is a leading cause of death, long-term disability, and cognitive impairment inflicting catastrophic consequences on patients and their families as well as placing a significant burden on the healthcare system and national economy. It is estimated that 795,000 people experience a stroke per year with approximately 610,000 first attacks and 185,000 recurrent attacks (Go et al., 2014). In real time every 40 seconds, someone experiences a stroke, and about every 4 minutes, someone dies from a stroke (Go et al., 2014). It is one of the most common reasons, second only to dementia, for nursing home admissions (Van Rensbergen & Nawrot, 2010). Direct spending on non-nursing home stroke care constitutes about 11% of the Medicare budget and close to 2% of overall national health expenditures (Ovbiagele et al., 2013). The long-term direct costs of nursing home care are even higher, and indirect costs from premature mortality and lost productivity for stroke victims are greater than all the costs combined (Demaerschalk, Hwang, & Leung, 2010). Taking all these costs into consideration, by 2030, the total annual costs of stroke are projected to increase to 240 billion dollars, an increase of 129% (Ovbiagele et al., 2013). These critical statistics underscore the need for new and improved stroke prevention strategies.

It is widely accepted that the most effective way to reduce the serious disease burden of stroke is to identify and aggressively control common individual risk factors such as smoking, hypertension, atrial fibrillation, diabetes, obesity, and hyperlipidemia (Goldstein et al., 2011). One other important modifiable stroke risk factor (SRF) that has emerged in research is obstructive sleep apnea (OSA). OSA is the repeated obstructive narrowing or closure of the upper airway during sleep leading to transient hypoxemia, arousals, and apneas. Apneas are measured per hour of sleep by the apnea hypopnea index (AHI) ranging from mild OSA level of 5 to severe OSA level of 30 or greater (Davis, Billings, Longstreth, & Khot, 2013). Continuous positive airway pressure (CPAP) is the gold standard treatment for OSA and works by counteracting the negative airway pressure created by the obstruction. The significance of OSA is that it not only directly contributes to several other SRFs but also has recently gained evidence as an independent SRF in and of itself. What makes OSA such a compelling SRF is its high prevalence in patients with stroke and transient ischemic attack (TIA) compared with the general population of approximately 4% (Meschia et al., 2014; Young, Peppard, & Gottlieb, 2002). One recent meta-analysis showed that 72% of patients with acute stroke/TIA exhibited OSA with an AHI of more than 5 (Johnson & Johnson, 2010). Therefore, identifying and treating OSA in patients with stroke/TIA offers a novel and much needed strategy to improve stroke prevention.

The 2014 American Heart Association/American Stroke Association (AHA/ASA) Primary Stroke Prevention Guidelines (SPG) continue to classify OSA as only a potentially modifiable risk factor, ranking it with much less prevalent and more remote stroke risks of migraine and drug abuse (Goldstein et al., 2011; Meschia et al., 2014). However, in the 2014 Secondary SPG, OSA has now been recognized as a prevalent risk factor, but not yet an independent SRF (Kernan et al., 2014). This was a welcomed improvement to the 2011 Secondary SPG where OSA was not mentioned in any context (Furie et al., 2011). Unfortunately though, the Secondary SPG recommendations for OSA screening and CPAP treatment are stated as “might be considered” but are not required (Kernan et al., 2014). In contrast, OSA was recognized as a major modifiable SRF in the 2012 Canadian Best Practice Recommendations for Stroke Care update (Coutts & Kelloway, 2012). Therefore, the twofold purpose of this article is, first, to present the research evidence that statistically supports the endorsement of OSA as an independent SRF with required screening and CPAP treatment in AHA/ASA SPG recommendations and, second, to describe unique opportunities for neuroscience nurses to improve stroke/TIA patient outcomes through OSA initiatives and engage in an OSA-sensitive nursing process that includes OSA assessment and interventions to advance best practices in stroke/TIA patient care.

METHODS

A systematic literature search using the Internet databases of Medline, CINAHL, and PubMed, including a manual review of reference lists, was conducted from September 2013 to February 2014 according to the recommended standards of Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 Statement (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group, 2009). The key search terms used were obstructive sleep apnea, sleep-disordered breathing, and stroke risk. A
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synthesis of the evidence was undertaken on research articles that were related to the risk, mortality, and prevalence relationship between OSA and stroke/TIA independent of other risk factors. This included research on neurological recovery and stroke recurrence for patients with stroke with OSA using CPAP therapy compared with those not treated, reinforcing the importance of required OSA screening and treatment recommendations in SPG. This literature review used a 10-year inclusion, 2003-2013, to show the accumulation of maturing evidence in this body of research. This was also emphasized in the 2014 Secondary SPG, which included literature dating as far back as 1995 (Kernan et al., 2014). Within this time span, large landmark epidemiology studies are appreciated that are referenced in the Heart Disease and Stroke Statistics 2014 Update and 2014 Secondary SPG (Go et al., 2014; Kernan et al., 2014). This review was based on rigorous inclusion and exclusion criteria to insure unbiased research selection, even stricter than the 2010 meta-analysis referenced in the 2014 Secondary SPG (Johnson & Johnson, 2010; Kernan et al., 2014). The inclusion criteria consisted of English-language research articles found in peer-reviewed journals involving both men and women older than 17 years old. Only studies that referred to OSA or sleep-disordered breathing by the OSA diagnostic criteria determined by AHI or respiratory distress index and measured by a standardized portable diagnostic system or overnight polysomnogram were included. Studies that tested CPAP treatment on patients with stroke must have used adherence criteria of greater than or equal to 4 hours per night for more than 70% of nights, which is the standard set by the National Coverage Determination of the Centers for Medicare and Medicaid Services (2013). Exclusion criteria consisted of expert opinion and consensus articles as well as other literature reviews or meta-analyses, using their results only to compare with the findings of this literature review. Studies were also excluded if the OSA screening was based only on self-reports, snoring history, or sleep questionnaires or if the study included less than 10 subjects.

RESEARCH RESULTS

From the 1,035 articles initially identified, 28 research articles were reviewed: 15 observational cohorts, five case-control studies, four cross-sectional studies, and four randomized control trials (RCTs), involving 10,671 subjects (Fig 1). Twelve different countries were represented in the studies with six articles from Spain; five from the United States; three from Canada; two from Australia, Germany, Korea, Poland, and Sweden; and one from Egypt, Switzerland, Malaysia, and Taiwan (Table, available as Supplemental Digital Content 1 at <http://links.lww.com/JNN/A66>). The Epworth Sleepiness Scale (ESS) was used in 16 of the 28 studies (57%) to test excessive daytime sleepiness commonly experienced by patients with OSA, but in most patients with stroke/TIA with OSA, excessive daytime sleepiness was not observed. OSA prevalence was evaluated in 23 studies involving 2,220 patients with stroke/TIA, and nine of the studies used ESS without eliciting positive ESS scores (Table 1). The AHI severity treatment levels varied in these studies, but the total weighted average percentage of OSA prevalence in patients with stroke/TIA was 68%. The most commonly used AHI treatment level was greater than or equal to 10, with the OSA prevalence averaged at 63% in 13 studies. Ten of 23 studies (43%) excluded patients who had been diagnosed with OSA before the stroke to emphasize the prevalence of undiagnosed OSA in patients with stroke/TIA. OSA as an OBSTRUCTIVE SLEEP APNEA AS AN INDEPENDENT STROKE RISK FACTOR: A REVIEW OF THE EVIDENCE, STROKE PREVENTION GUIDELINES, AND IMPLICATIONS FOR NEUROSCIENCE NURSING PRACTICE

independent SRF or mortality risk was analyzed in six observational cohorts, three cross-sectional studies, and two case-controlled studies, with 82% documenting statistically significant positive findings. One observational cohort study showed that stroke patients with OSA at AHI equal to or greater than 15 are at a 75% higher increased risk for early death (Sahlin et al., 2008). Age and obesity, measured by body mass index (BMI), were the most commonly adjusted factors and statistically controlled in 9 of the 11 studies, reinforcing OSA as an independent SRF in most of the studies. Consistent with the conclusions of the 2014 Secondary SPG and a recent meta-analysis, most patients with stroke/TIA were found to have lower BMI scores than the general OSA population (Go et al., 2014, Johnson & Johnson, 2010). All seven of the CPAP therapy studies showed reduction in stroke recurrence and mortality as well as improved neurological recovery than those patients who were not treated with CPAP, with 71% as statistically significant. The RCT using CPAP-trained nurses to administer CPAP in a stroke rehabilitation unit was the only study that achieved 100% acceptable adherence (Ryan et al., 2011). Three studies examined the OSA relationship with stroke severity, functional capacity, and length of stay. One observational cohort study found that, when AHI was greater than 10, there was a corresponding increase in stroke severity measured by the National Institutes of Health Stroke Scale (Rola et al., 2007). Another case-control study showed decreased functional capacity by 2.3 on the Functional Independence Measure for every increase of 10 AHI units and that the combined length of stay was 16 days (30%) longer in a hospital and rehabilitation facility and 14 days longer (40%) in a rehabilitation facility alone (Kaneko et al., 2003).

DISCUSSION

The results of this literature review correlate with other recent literature reviews and meta-analyses, all of which show a consistent association of OSA with increased risk of stroke independent of other SRFs (Das & Khan, 2012, Dong, Zhang, & Qin, 2013, Johnson & Johnson 2010, Loke, Brown, Kwok, Niruban, & Myint, 2012). The Sleep Heart Health Study was the largest epidemiological study, involving 5,422 diverse community-based participants prospectively followed for over 8 years, that revealed statistically strong evidence that OSA increases the risk of first-time stroke, specifically in men (Redline et al., 2010). Men with moderately severe OSA had about a threefold increased risk of ischemic stroke with an escalating stroke risk by 6% with every unit increase in baseline AHI from 5 to 25 (Redline et al., 2010). This level of stroke risk is comparable with atrial fibrillation, which is estimated to increase the risk of stroke by about threefold as well (Redline et al., 2010; Sacco et al., 2001). Another recent prospective study involving 293 Korean patients with ischemic stroke found OSA with AHI 10 or higher to be very common with a prevalence of 63% (Ahn et al., 2013). Factoring in the different stroke risk profiles of these patients, along with a higher incidence of wake-up stroke, suggested that OSA is an independent risk factor for stroke (Ahn et al., 2013). Another smaller prospective study showed not only that patients with wake-up stroke had more severe OSA but that the risk for wake-up stroke in patients with severe OSA was six times higher than those without severe OSA (Hsieh et al., 2012). Wake-up stroke is particularly important to prevent because the time of stroke onset cannot be determined and disqualifies these patients from receiving the only Federal Drug Administration-approved acute

treatment for stroke, tissue plasminogen activator (tPA), within 3 hours of onset. Under stricter criteria, tPA is recommended to give up to 4.5 hours, although it is not Federal Drug Administration approved (Jauch et al., 2013). However, even with this extended time limit, most patients with wake-up stroke are still disqualified.

This literature review also identified substantial evidence that patients with stroke treated with CPAP had positive effects on their neurological impairment recovery and mortality outcomes compared with those not treated, who had much poorer outcomes. In a 2011 RCT, a 14% absolute increase in functional outcome was appreciated with the National Institutes of Health Stroke Scale score reduced by 3 points (Bravata et al., 2011). This is a compelling finding when compared with the National Institute of Neurological Disorders and Stroke study that validated tPA treatment by showing an 11% absolute increase in functional outcome at 3 months poststroke (National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group, 1995). Furthermore, there is consistent evidence in all the studies that most patients with stroke/TIA have less OSA-associated daytime sleepiness and obesity compared with patients with nonstroke OSA, rendering the usual clinical screening tools of the ESS and BMI insufficient when used alone. CPAP adherence is challenging, and specialized support for troubleshooting and deconditioning strategies is necessary for beneficial adherence. The researchers of the RCT who showed statistically significant neurological improvements with CPAP stated that 100% compliance was achieved because of the fact the subjects were supported by CPAP-trained nurses in a stroke rehabilitation unit (Ryan et al., 2011). Research bias was evaluated in all the studies with most limitations related to small sample size, with 54% of the studies having less than 100 subjects, and CPAP intolerance contributed to this limitation.

CONCLUSION

Stroke is responsible for major disability, significant mortality, and escalating healthcare costs. New prevention strategies are desperately needed. The 2014 AHA/ASA Secondary SPG have made progress in recognizing OSA as a prevalent risk factor with new considerations for OSA screening and treatment. However, the evidence presented in this literature review, as well as others, supports recognizing OSA as an independent SRF in the AHA/ASA SPG just as Canada has done. Recognition of OSA as an independent SRF would change healthcare practitioners' behavior by requiring, rather than simply considering, OSA screening and treatment. OSA identification and treatment in patients with stroke/TIA will significantly improve secondary stroke prevention and neurological impairment recovery. The two highlighted OSA initiatives have illustrated the effectiveness of nurse-led clinical, educational, and quality improvement interventions to identify and treat OSA in hospitalized patients. Neuroscience nurses are positioned to champion OSA initiatives and promote best practices in stroke/TIA patient care by engaging in an OSA-sensitive nursing process. Neuroscience nurses who capitalize on these unique opportunities will improve stroke patient outcomes and thereby have an enormous impact on reducing the physical, financial, and social burden of stroke on patients, their families, and society at large.

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