

Obstructive Sleep Apnea in the Elderly Population: Atypical Presentation and Diagnostic Challenges

H Ganga, Y Thangaraj, V Puppala, N Kolla

Citation

H Ganga, Y Thangaraj, V Puppala, N Kolla. *Obstructive Sleep Apnea in the Elderly Population: Atypical Presentation and Diagnostic Challenges*. The Internet Journal of Internal Medicine. 2009 Volume 8 Number 2.

Abstract

OSA impacts every aspect of daily functioning in the elderly population. Obstructive sleep apnea is widely prevalent in the elderly population yet it is underdiagnosed due to factors such as lack of awareness of the condition and atypical presentation of the disorder. Understanding the atypical presentation of obstructive sleep apnea in the elderly population is vital for the early diagnosis and health care cost control as this disorder causes wide variety of disease affecting cardiovascular, pulmonary and central nervous systems. Furthermore, it affects the psychological status and the social well being of the elderly population.

INTRODUCTION

Obstructive Sleep Apnea (OSA) has emerged as an important separate entity with extensive research and studies done in the past two decades. Traditional risk factors such as obesity, body mass index (BMI), neck circumference and snoring are less prevalent in the elderly population leading to diagnostic challenges and confusion among the health care providers.

As the percentage of the elderly population rises, this group demands separate

careful analysis as OSA presents across a broad spectrum. Increasing numbers of geriatric patients are seen by internists and family medicine physicians. This pattern is only going to increase due to the rapid advances in the medical field extending the life expectancy by decades. The approach to this group cannot be similar to the middle-aged and the younger age groups. One study already stated that OSA is underdiagnosed in the elderly age groups (1). Tarasiuk et al. (2) compared the healthcare utilization and morbidity of the elderly population with OSA with elderly subjects without OSA and middle-aged subjects with OSA. They found that elderly patients with OSA have high health care utilization due to associated cardiovascular morbidity and use of psychoactive medications. Hence they stated that the clinical significance of OSA in the elderly population is high.

In a study done to find out the determinants of health care utilization in OSA patient population, age more than 65

years and female gender were the leading elements that predicted most costly OSA patients (3). The same study reported that it was not the patients with high BMI or classic OSA severity indices such as arousal index that predicted high healthcare utilization.

The goal of this review is to bring to attention the wide spectrum of the atypical features of OSA in the elderly population, understanding the basis for underdiagnosis of OSA in the elderly population and look for cost-effective clinical solutions for diagnosing OSA in the elderly population.

PREVALENCE OF OSA IN THE ELDERLY POPULATION

The prevalence of sleep disordered breathing (SDB) in the older adults is between 20 % to 50% (4). The prevalence of sleep disorders increases with the age, with the elderly population between 70 to 80 years having almost twice the percentage of those around the age of 40 years (5). The fact that there are large numbers of undiagnosed elderly patients with OSA in the community has to be considered while taking these percentages into account. Multiple reasons account for the underdiagnosis of OSA in the elderly; atypical presentation, cognitive issues, reluctance to report, lack of data about the criteria for identifying the disorder and lack of awareness of this entity among the physicians are the important reasons.

EFFECT OF OSA ON MORBIDITY, MORTALITY

AND PRODUCTIVITY

The widespread impact of OSA indicates the significance and the impending epidemic like situation medical field could face if this entity is ignored. The association of OSA with wide spectrum of diseases such as hypertension (6, 7), congestive heart failure (8, 9), stroke (10), coronary artery disease (8, 11), atrial fibrillation (12) is concerning as these diseases are the leading causes of mortality in the elderly population.

The role of OSA in the daytime sleepiness and impaired cognitive ability with subsequent increased risk of motor vehicle accidents is concerning (13). Studies done worldwide have noted increased risk and incidence of traffic accidents in people with sleep disorders especially sleep apnea (14-23). The National Report of Sleep-Related Accidents submitted to the United States Government in 1994 estimated that roughly 23000 deaths and 25000000 disabling injuries occur due to the sleep-related accidents. The study estimated the costs to be as high as 56 billion and this was back in 1995 (24). Patients with OSA are more likely to be somnolent, anxious, depressed, and have lower level of vigilance (25, 26). Teran-Santos et al. showed that there is a strong association between sleep apnea and the risk of traffic accidents (27). Sleep apnea is also responsible for the occupational accidents and impaired work performance (28-30).

OSA worsens hypertension (HTN), causes variation in blood pressure readings and increases the risk for nocturnal HTN (7). Coy et al. reported that OSA is related to diastolic blood pressure (31). OSA is considered to be a risk factor for the genesis of HTN, though the mechanism for this is not clear (32). OSA is a risk factor for stroke and death (33, 34). Tosun et al. reported that the prevalence of OSA in stroke patients is almost 74% (35).

OSA was found to be in high prevalence in patients with acute myocardial infarction and coronary artery disease (36-38). OSA helps in identifying the patients at risk for coronary artery disease (CAD) and could be a modifiable risk factor (36). Gami et al. have shown that the patients with OSA are more likely to have family history of premature CAD than those without OSA (39). OSA has been described as a risk marker for CAD (40).

Studies noted that OSA could be a risk factor for congestive heart failure (CHF) (41, 42). Roughly half the patients with CHF have sleep breathing disorders, with variable proportions of central and obstructive patterns of sleep apnea

(43). Severe hypoxemia in OSA could cause nocturnal angina and exacerbation of CHF (44). OSA has been shown to be an independent risk factor for the new-onset atrial fibrillation (AF) (45).

However, recently Martinez-Garcia et al. reported that OSA has very little impact on the quality of life in the elderly. This finding was in contrast to what they found in the age groups below 65 years of age (46).

CLINICAL FEATURES OF OSA IN THE ELDERLY PATIENT POPULATION

While the prevalence of sleep apnea is much higher in the elderly population (5), less is known about how we can predict or suspect OSA clinically in the elderly population. Traditional symptoms of OSA have been snoring, daytime sleepiness. Men are twice likely as women to have sleep-disordered breathing (SDB), however this difference is not seen after the menopause (13). Traditional signs include overweight and obesity, high basal metabolic index (BMI), large neck circumference, craniofacial and upper airway abnormalities (47). However in the elderly, studies have shown that the association of OSA with these traditional signs and symptoms is not significant. In a classic study that has widespread implications, Enright et al. showed that snoring is inversely related to age in the elderly patients (48). In the Sleep Heart Health Study, the prevalence of snoring and breath pauses was low in the participants over the age of 70 years (49).

Cherniak et al. in a recent study reported that OSA and the metabolic syndrome are interrelated (50). They hypothesize that obesity and anatomic changes in upper airways could be closely involved with the pathways responsible for neural control of breathing to cause hypoxia. Homocysteine levels were found to be elevated in the elderly patients with OSA syndrome and the reason for this elevation could be oxidative stress (51).

In an other study involving the elderly hypertensive patients with OSA, it was found that OSA patients had significantly elevated levels of fasting and postprandial glucose levels, hemoglobin A1C, total cholesterol, low density lipoprotein, triglycerides compared to the group without OSA (52). Daytime sleepiness could lead to confusion, if relied upon as diagnostic criteria for the elderly patients. At present it is not clear, if we can attribute daytime hypersomnolence to OSA, without considering factors such as neurocognitive deficits, destructured sleep in general in the older population, the effects of polypharmacy and prevalence of multiple

comorbidities (53, 54).

Obesity is also a poor predictor of OSA in the elderly population with conflicting evidence so far. Increased BMI has been shown to be predictive of OSA in both the middle-aged and the older adults (4, 47). Contrarily, obesity has been shown to have a weak association with OSA in the elderly population by Endeshaw (1). In a recent interesting study (55), Chung et al. compared the effects of age on the endothelial dysfunction and the inflammatory responses of OSA. They found that the C-reactive protein (CRP) levels in the middle aged groups were affected by the BMI and the waist to hip ratio whereas in the elderly, CRP levels were affected by the apnea hypopnea index (AHI). Hence they concluded that cardiovascular risks were predicted by obesity in the middle aged groups and nocturnal respiratory changes in the elderly groups. Wang et al. reported that elderly patients with OSA have higher incidences of cardiovascular complications and hypertension compared to the middle aged groups (56).

Hypoxia-induced oxidative stress has been explained as the reason behind the increased inflammatory mediators like cytokines, adhesion molecules leading to increased cardiovascular events in the elderly population with OSA (57). Endeshaw et al. pointed that there may be an association between edentulism and OSA in the elderly population (58).

Kobayashi et al. in a recent article compared the clinical features between the elderly patients with middle-aged onset OSA and the elderly with old age onset OSA(59). Patients with elderly onset OSA syndrome had lower frequency of arousal compared to the elderly with middle-aged onset OSA syndrome.

Apart from the above presentations, OSA can be very diverse and distinct in the elderly population by presenting as nocturia, recurrent falls, cognitive impairment, choking, impaired driving ability and traffic accidents (54). True sleep disorders are far less prevalent in healthy older adults and if present are associated with co-morbidities. Sleep disorders are more likely to be found in people with greater risk of dementia such as the elderly population and patients with cognitive impairment (60). OSA presents most commonly as excessive daytime sleepiness (61). This could be one of the major factors involved in cognitive impairment which further causes social problems like traffic accidents and work place accidents. Severe OSA affects the neural activation and responses involved in working memory (62).

Interesting findings have been reported by

Mazza et al. regarding attention span of OSA patients. They mention that OSA patients apart from having difficulty to stay awake in monotonous situations, struggle to maintain attention in stimulating conditions (63). This study was done in general population and can be attributed to the elderly population. They found that 95% of the study population of OSA patients had attention and vigilance problems. OSA patients have trouble with executive cognition control and motor coordination abilities (64). Bedard et al. using neuropsychological assessment found that OSA patients have psychomotor deficits due to severity of hypoxemia and attention and memory deficits due to vigilance problems (64). Elderly OSA patients reported falling-asleep-related injured falls and recurrent fall history (65). OSA patients involved in traffic accidents are likely to have severe OSA syndrome, excessive daytime sleepiness and lower quality of life (66). OSA patients are more likely to have traffic accidents (odds ratio 6.3, 95 percent confidence interval 2.4 to 16.2) compared to the general population even after adjusting for alcohol use, body mass index, visual problems, driving experience, medication effects (27). Mulgrew et al. (67) in an interesting study, reviewed objective crash data, nature of accidents and severity for 783 patients with suspected OSA for 3 years prior to polysomnography (PSG). They compared this data with 783 age and sex-matched controls. They report that OSA patients not only have higher risk of motor vehicle accidents (MVA) but also have increased rates of motor vehicle accidents involving personal injuries. They found that very severe motor vehicle accidents (head-on collisions, involving pedestrians) were rare in their study group, but 80 % of such accidents occurred in patients with OSA.

Interesting findings have been reported regarding the role of OSA in vision abnormalities. It has been reported to cause Non-arteritic Anterior Ischemic Optic Neuropathy (NAION) (68, 69). A recent study from Brazil has reported that sleep apnea has greater negative impact on sexual activity and erectile function in the elderly population compared to the younger population (70).

REASONS FOR ATYPICAL PRESENTATION OF OSA IN THE ELDERLY POPULATION

The presentation of OSA in the elderly population is varied and has been subject of interest for multiple studies. The diverse and atypical presentation led the clinicians to consider if OSA is a distinct entity in the elderly population

(54). There is a serious need to figure the cardiovascular risk factors of OSA syndrome in the elderly population as the majority of studies in sleep apnea have been done in the middle-aged population (55).

Several studies mention that anatomic reasons could be behind the cause of atypical presentation in the elderly population. The role of pharyngeal diameter as a cause and atypical presentation of OSA has been described by multiple studies with contradicting results. Malhotra et al. mentioned that age influences the pharyngeal musculature (71). They mention that with aging, there is a decrease in negative pressure reflex in men, preferential deposition of parapharyngeal fat irrespective of obesity, in both sexes and pharyngeal lengthening in women. The study mentions an important finding that age-related increased deposition of parapharyngeal fat in both men and women occurs independently of BMI and obesity. This finding also explains that it is easy to overlook OSA in the elderly population if one is looking at obesity as a risk factor. A change in bone shape surrounding pharynx was also observed with the aging. Soft palate length was found to be increased in women with aging. Increased pharynx length increases the risk of pharyngeal collapse (72). Several studies in the past have mentioned that aging alters the pharyngeal anatomy or functioning of the pharyngeal dilator muscles, increasing the risk for apnea in the elderly population (73-76).

A recent study by Enciso et al. (77) compared the CT scan findings in a prospective study between patients with OSA with apnea hypopnea index (AHI) > 10 events/hour and snorers with AHI < 10 events/hour. This study compared the upper airway morphology between the two groups and found that the presence and severity of OSA increases with increasing age and narrow upper airway lateral dimensions (< 17 mm). They also found that patients over the age of 57 years were 3.5 times more likely to have OSA.

Loss of teeth and the use of denture have been explained as a possible cause of OSA in the elderly (58). In a case report, cervical spine osteophytes have been reported as cause of obstruction causing OSA in a 75 year male (78).

Physiologic events have also been explained as a cause for distinct presentation in the elderly patients. In a recent study, smaller intrathoracic pressure has been explained as the reason for elderly requiring lower levels of CPAP (59). The decrease of compliance of the upper airway with the age has been explained as a cause for OSA in the elderly population

(76). Chemo sensitivity to hypoxia and hypercapnea can decrease with the age and this can contribute to OSA in the elderly patients and cause atypical presentation (59).

Oxidative stress has been explained to have a role in causing OSA in the elderly by causing an increase in the homocysteine levels (51, 57).

Kobayashi et al. mention that the clinical significance of OSA in the elderly without obesity appears to be mild (59). The overlap of OSA with insomnia is another diagnostic challenge. Beneto et al. mention that the relation between OSA and insomnia disorder is bidirectional. OSA could cause insomnia thorough psychophysiological conditioning due to sleep fragmentation and dysfunctional sleep behaviors. Insomnia can contribute to OSA by altering the upper airway muscle tone due to sleep disturbances. The study also mentions that the interaction between insomnia and OSA could be due to an increase in the hypothalamic-pituitary-adrenal (HPA) axis activity (79).

Sleep studies done in general population reported that patients with OSA have decreased brain activation in the cingulate, frontal and parietal regions typically involved in attention tasks (80). The underlying cause for neurocognitive problems in the elderly with OSA could be sleep loss with the additive effects of age factor and increased prevalence of dementia. Furthermore, age-related memory loss could be involved in neurocognitive deficits in the elderly patients with OSA. Use of psychoactive medications can further increase the risk of attention, cognition and falls in the elderly population (2).

Onen et al. reported for the first time the causal relationship between excessive sleepiness due to OSA and recurrent falls (65). In the same paper, the author also explains the connection between cognitive status, attention and the increased risk of fall in the elderly. Gait could be an extension of higher level of cognitive ability as it involves complex interaction between attention, planning, memory and execution of motor functions. Hence the interplay of multiple factors like lack of sleep, cognitive dysfunction, attention span, psychomotor dysfunction could be responsible for falls in the elderly population (65).

The effect of multiple medications, disease-disease interactions are other factors that could cause atypical presentation of OSA in the elderly (1). Low prevalence of snoring in the elderly population could mask the presentation of OSA (49). The absence of partner could complicate the diagnosis of OSA as patients may report

negatively to the question whether they snore. The reason for this negative answer to the snoring question is due to the fact that these individuals may not have any one to tell them that they snore (1).

DIAGNOSTIC CHALLENGES

There is no clear consensus on the clinical features and the criteria for diagnosing OSA in the elderly. There is increasing dearth of physicians in this specialty and this factor is additionally complicating the situation. Identifying occult OSA in the elderly population will require a different approach as they have wider spectrum of presentation. Recent report that OSA can present with structural changes such as gray matter loss in cerebrum, before manifesting as neuropsychological symptoms is concerning (81). Untreated OSA increases the risk of cardiovascular, cerebrovascular disorders, HTN substantially, apart from being a cause of social dysfunction, poor quality of life and decreased productivity (82).

Polysomnogram (PSG) is the gold standard for diagnosing OSA to date. However this test is costly, time consuming, technically demanding, labor intensive and cannot be applied as a screening tool on a mass level for large populations. Ambulatory devices may be less costly, easier to operate and as good as PSG in identifying OSA patients in the community (83). These devices may be practical to use and economical inspite of some disadvantages. One study points out that ambulatory device such as Embletta; Venla can show false negative diagnosis in mild OSA. This indicates that diagnostic accuracy may be instrumentation dependent (84).

The fact that 85-90% of patients in the overall population with OSA are undiagnosed is concerning and reasons for the underdiagnosis could be poor suspicion of the disorder apart from lack of awareness (82). Epworth Sleepiness Scale (ESS) has been used to diagnose daytime sleepiness and sleep disorders but the validity of this scale use in the geriatric population is questioned as it relies on cognitive status and memory to answer the questions (85). Thus, clinical knowledge and the suspicion of the OSA play a key role for identifying OSA before using devices to confirm the suspected diagnosis.

In an important study, Onen et al. (85) devised a simple bedside tool called observation-based nocturnal sleep inventory (ONSI) to examine a greater number of the elderly people with sleep apnea syndrome (SAS) and optimize the use of PSG. The ONSI is based on the nursing observations

in 5 standardized hourly visits in one night. The criteria include observation of three important characteristics of sleep disordered breathing (SDB): gasping, choking or interrupted breathing (apnea); snoring; and awakening. ONSI had high sensitivity (90%), specificity (80%), was low in cost and easy to use in screening the older adults for SAS . It can be used to identify and triage the elderly patients with OSA, considering the high prevalence of OSA in this age group. ONSI tool was superior to physician suspicion and slightly inferior to the standard PSG in diagnosing OSA.

Wang et al. compared the clinical and polysomnographic characteristics of the elderly patients and the middle-aged patients in the Chinese population and came out with some interesting findings (56). The study found that elderly patients were found to have lower apnea hypopnea index (AHI), snoring index, body mass index (BMI) compared to the middle-aged group. Elderly patients were also found to have worse sleep architecture disturbance.

Identifying the high risk population such as patients with HTN, CHF may help in localizing OSA better (86). Understanding the pattern of presentation and the reasons for atypical presentation will help physicians deal with OSA better in the elderly population. It is very important to remember there is minimal or no relation between OSA and self reporting of sleepiness and snoring in the elderly populations (48, 87-90). When an elderly person presents with either coronary event, stroke, repeated falls or has traffic accident, it is prudent to consider OSA as a part of the differential diagnosis and pursue it if other causes seem to be less likely. Clinical suspicion is a major tool until we have clearly defined practice guidelines. It is important to consider OSA in the high risk groups early and initiate treatment (91).

TREATMENT OPTIONS

CPAP (continuous positive airway pressure) is the standard treatment for OSA in the elderly and the middle-aged population. Numerous studies have noted the benefits of treating OSA with CPAP in the middle-aged and the elderly population. In one study the elderly-onset OSA group required lower levels of CPAP compared to middle-age onset OSA group (59). Treating with the CPAP can help treat underlying cardiovascular disorders (92). Oktay et al. reported that if OSA patients meet the criteria of metabolic syndrome (MS), they should be treated with CPAP therapy to prevent the development of the cardiovascular disease (93). Long-term CPAP therapy can reduce the mortality in

patients with CPAP and ischemic stroke (94). CPAP can reduce hypertension in patients with OSA (95). CPAP has also been shown to increase survival in COPD patients in oxygen (96). CPAP treatment has shown benefit with OSA patients with erectile dysfunction by improving the sexual function (97). CPAP therapy reduces the degree of daytime sleepiness (98). Newer modalities such as C-Flex, A-Flex and APAP are being used but their benefits are yet to be validated (99).

Treatment with CPAP results in improved daytime vigilance, attention and consequently gait and balance preventing falls in elderly (65).

Multiple studies have been done to evaluate the benefits of CPAP treatment in cognitive impairments. General cognitive functioning improved with CPAP treatment (100). One study reported that CPAP therapy when used for short duration (<2 weeks) helps in the improvement of vigilance, alertness and attention while longer duration of treatment may be needed for overall cognitive improvement (101). Sanchez et al. from their recent comprehensive literature search on the benefit of CPAP therapy on the cognitive dysfunction of the OSA patients report that the results are not consistent. This inconsistency in the results is due to a combination of factors such as adherence and tolerance to therapy, insensitive neuropsychological assessment, variability in the sample and the severity of OSA patients (102).

Treatment with CPAP helps in prevention of motor vehicle accidents in OSA patients (103, 104). One study states that CPAP therapy prevents traffic accidents, reduces subsequent health care costs, improves quality of life and is an efficient way of using healthcare resources (105). Mazza et al. reported that after CPAP treatment , there is no longer any difference between OSA patients and normal subjects in their attention and driving performance (106).

CPAP slows deterioration of sleep, cognition, mood in patients with Alzheimer's disease and OSA (107). One study recommends clinicians to consider CPAP therapy in patients with Alzheimer's dementia and OSA for improving the cognitive dysfunction (108).

Surgical modalities are considered in patients who have failed or are intolerant to the conventional OSA therapy. Maxillomandibular advancement has high surgical efficacy rate of 86% and cure rate of 43% (109).

Uvulopalatopharyngoplasty (UPPP) is a soft palate surgical

technique with surgical efficacy of 50% and cure rate of 16% (109, 110). UPPP has been shown to be safe in patients who have failed the CPAP therapy (111).

CONCLUSION

The impact of OSA in the elderly population is far reaching, in terms of the effects it has on the morbidity, mortality and the quality of life. The presentation of OSA in such a diverse way suggests that its prevalence is much more than what we are aware of. The economic impact is staggering (112). As the numbers of the elderly population increase, the prevalence and significance of OSA will also increase, demanding greater attention and allocation of the financial resources. OSA affects every aspect of life and daily functioning in the elderly population. OSA increases the risk of CAD, CHF, Stroke (8, 113, 114). The indirect costs, morbidity and mortality have to be considered in such a scenario. Healthcare utilization of the elderly patients with OSA is high due to associated cardiovascular morbidity and use of psychoactive medications (2). They are among the costliest OSA patients to manage and heavy users of health-care resources (3).

The diverse nature of the elderly population makes it challenging to diagnose and apply uniform clinical criteria. Many of the symptoms of OSA in the elderly are also caused by other disorders which are common in elderly such metabolic syndrome, cardiovascular disorders and this factor makes OSA furthermore difficult to diagnose (50). At the same time, underdiagnosis of such a condition increases the burden of diseases and costs for the society. Treating OSA with CPAP can help treat refractory HTN, depression, fatigue, decrease traffic accidents, improve work efficiency and productivity, decrease the incidence of stroke, CHF, CAD, improves the quality of life thereby saving huge costs for the society in the near long term (8, 94, 115-118).

The most important factor seems to be the lack of awareness among the physicians regarding the prevalence and the impact of OSA (119, 120) . To complicate this further, atypical presentation of OSA in the elderly population makes it harder to diagnose this highly prevalent disease. While it is hard to confine the diagnostic criteria of OSA to a set of clinical features in the elderly patients, it is prudent to have a set of clinical features and cheaper screening tools such as ONSI to diagnose the suspected groups. Application of sleep neuroimaging may also help us to identify this disorder faster and earlier before it causes clinical symptoms (121). Studies are needed to help us identify the set of high risk

clinical features of OSA. But the urgent issue is spreading the awareness of this epidemic in the health-care providers and the elderly population.

References

1. Endeshaw Y. Clinical characteristics of obstructive sleep apnea in community-dwelling older adults. *J Am Geriatr Soc.* 2006 Nov;54(11):1740-4.
2. Tarasiuk A, Greenberg-Dotan S, Simon-Tuval T, Oksenberg A, Reuveni H. The effect of obstructive sleep apnea on morbidity and health care utilization of middle-aged and older adults. *J Am Geriatr Soc.* 2008 Feb;56(2):247-54.
3. Tarasiuk A, Greenberg-Dotan S, Brin YS, Simon T, Tal A, Reuveni H. Determinants affecting health-care utilization in obstructive sleep apnea syndrome patients. *Chest.* 2005 Sep;128(3):1310-4.
4. Ancoli-Israel S, Kripke DF, Klauber MR, Mason WJ, Fell R, Kaplan O. Sleep-disordered breathing in community-dwelling elderly. *Sleep.* 1991 Dec;14(6):486-95.
5. Young T, Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. *Arch Intern Med.* 2002 Apr 22;162(8):893-900.
6. Baguet JP, Barone-Rochette G, Pepin JL. [Obstructive sleep apnea syndrome, hypertension and artery]. *Presse Med.* 2009 Apr;38(4):627-32.
7. Friedman O, Logan AG. The price of obstructive sleep apnea-hypopnea: hypertension and other ill effects. *Am J Hypertens.* 2009 May;22(5):474-83.
8. Butt M, Dwivedi G, Khair O, Lip GY. Obstructive sleep apnea and cardiovascular disease. *Int J Cardiol.* 2010 Feb 18;139(1):7-16.
9. Chowdhury M, Adams S, Whellan DJ. Sleep-disordered breathing and heart failure: focus on obstructive sleep apnea and treatment with continuous positive airway pressure. *J Card Fail.* 2010 Feb;16(2):164-74.
10. Munoz R, Duran-Cantolla J, Martinez-Vila E, Gallego J, Rubio R, Aizpuru F, et al. Severe sleep apnea and risk of ischemic stroke in the elderly. *Stroke.* 2006 Sep;37(9):2317-21.
11. Luthje L, Andreas S. Obstructive sleep apnea and coronary artery disease. *Sleep Med Rev.* 2008 Feb;12(1):19-31.
12. Braga B, Poyares D, Cintra F, Guilleminault C, Cirenza C, Horbach S, et al. Sleep-disordered breathing and chronic atrial fibrillation. *Sleep Med.* 2009 Feb;10(2):212-6.
13. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med.* 2002 May 1;165(9):1217-39.
14. Vennelle M, Engleman HM, Douglas NJ. Sleepiness and sleep-related accidents in commercial bus drivers. *Sleep Breath.* 2010 Feb;14(1):39-42.
15. Przybylowski T, Korczynski P, Broczek K, Rzadkiewicz E, Bielicki P, Zimnoch P, et al. [Drivers with obstructive sleep apnea as potential authors of car accidents]. *Pol Arch Med Wewn.* 1999 Aug;102(2):691-6.
16. George CF, Nickerson PW, Hanly PJ, Millar TW, Kryger MH. Sleep apnoea patients have more automobile accidents. *Lancet.* 1987 Aug 22;2(8556):447.
17. Findley LJ, Unverzagt ME, Suratt PM. Automobile accidents involving patients with obstructive sleep apnea. *Am Rev Respir Dis.* 1988 Aug;138(2):337-40.
18. Haraldsson PO, Carenfelt C, Diderichsen F, Nygren A, Tingvall C. Clinical symptoms of sleep apnea syndrome and automobile accidents. *ORL J Otorhinolaryngol Relat Spec.* 1990;52(1):57-62.
19. Findley LJ, Levinson MP, Bonnie RJ. Driving performance and automobile accidents in patients with sleep apnea. *Clin Chest Med.* 1992 Sep;13(3):427-35.
20. Stoohs RA, Guilleminault C, Itoi A, Dement WC. Traffic accidents in commercial long-haul truck drivers: the influence of sleep-disordered breathing and obesity. *Sleep.* 1994 Oct;17(7):619-23.
21. Horne JA, Reyner LA. Sleep related vehicle accidents. *BMJ.* 1995 Mar 4;310(6979):565-7.
22. Melazzini M, Braghioli A, Barone C, Donner CF. [Sleep disordered breathing: a new risk factor for accidents]. *G Ital Med Lav Ergon.* 2000 Apr-Jun;22(2):139-43.
23. Schlessier M, Tietze J, Leyen P, Knauf-Hubel D, Nati R. [Sleep apnea syndromes and traffic accidents]. *Bull Soc Sci Med Grand Duché Luxemb.* 2000(1):31-8.
24. Webb WB. The cost of sleep-related accidents: a reanalysis. *Sleep.* 1995 May;18(4):276-80.
25. Barbe P, Pericas J, Munoz A, Findley L, Anto JM, Agusti AG. Automobile accidents in patients with sleep apnea syndrome. An epidemiological and mechanistic study. *Am J Respir Crit Care Med.* 1998 Jul;158(1):18-22.
26. Ong JC, Gress JL, San Pedro-Salcedo MG, Manber R. Frequency and predictors of obstructive sleep apnea among individuals with major depressive disorder and insomnia. *J Psychosom Res.* 2009 Aug;67(2):135-41.
27. Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J. The association between sleep apnea and the risk of traffic accidents. Cooperative Group Burgos-Santander. *N Engl J Med.* 1999 Mar 18;340(11):847-51.
28. Accattoli MP, Muzi G, dell'Osso M, Mazzoli M, Genovese V, Palumbo G, et al. [Occupational accidents, work performance and obstructive sleep apnea syndrome (OSAS)]. *G Ital Med Lav Ergon.* 2008 Jul-Sep;30(3):297-303.
29. Ulfberg J, Carter N, Edling C. Sleep-disordered breathing and occupational accidents. *Scand J Work Environ Health.* 2000 Jun;26(3):237-42.
30. Rodenstein D. Sleep apnea: traffic and occupational accidents--individual risks, socioeconomic and legal implications. *Respiration.* 2009;78(3):241-8.
31. Coy TV, Dimsdale JE, Ancoli-Israel S, Clausen JL. The role of sleep-disordered breathing in essential hypertension. *Chest.* 1996 Apr;109(4):890-5.
32. Richert A, Ansarin K, Baran AS. Sleep apnea and hypertension: pathophysiologic mechanisms. *Semin Nephrol.* 2002 Jan;22(1):71-7.
33. 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 Nov 10;353(19):2034-41.
34. Sahlin C, Sandberg O, Gustafson Y, Bucht G, Carlberg B, Stenlund H, et al. Obstructive sleep apnea is a risk factor for death in patients with stroke: a 10-year follow-up. *Arch Intern Med.* 2008 Feb 11;168(3):297-301.
35. Tosun A, Kokturk O, Karata GK, Ciftci TU, Sepici V. Obstructive sleep apnea in ischemic stroke patients. *Clinics (Sao Paulo).* 2008 Oct;63(5):625-30.
36. Sorajja D, Gami AS, Somers VK, Behrenbeck TR, Garcia-Touchard A, Lopez-Jimenez F. Independent association between obstructive sleep apnea and subclinical coronary artery disease. *Chest.* 2008 Apr;133(4):927-33.
37. Lee CH, Khoo SM, Tai BC, Chong EY, Lau C, Than Y, et al. Obstructive sleep apnea in patients admitted for acute myocardial infarction. Prevalence, predictors, and effect on microvascular perfusion. *Chest.* 2009 Jun;135(6):1488-95.
38. Kong L, Guo XH. [The relation between obstructive sleep apnea hypopnea syndrome and the severity of coronary

- atherosclerosis in coronary artery disease]. Zhonghua Nei Ke Za Zhi. 2009 Aug;48(8):638-42.
39. Gami AS, Rader S, Svatikova A, Wolk R, Herold DL, Huyber C, et al. Familial premature coronary artery disease mortality and obstructive sleep apnea. Chest. 2007 Jan;131(1):118-21.
40. Schafer H, Koehler U, Ewig S, Hasper E, Tasci S, Luderitz B. Obstructive sleep apnea as a risk marker in coronary artery disease. Cardiology. 1999;92(2):79-84.
41. Yoneyama K, Osada N, Shimozato T, Ishibashi Y, Hayashi A, Takahashi E, et al. Relationship between sleep-disordered breathing level and acute onset time of congestive heart failure. Int Heart J. 2008 Jul;49(4):471-80.
42. Naughton MT. The link between obstructive sleep apnea and heart failure: underappreciated opportunity for treatment. Curr Heart Fail Rep. 2006 Dec;3(4):183-8.
43. Escourrou P, Nedelcoux H, Monti A, Medigue C. [Obstructive sleep apnea syndrome and heart failure]. Rev Neurol (Paris). 2001 Nov;157(11 Pt 2):S38-41.
44. Chan HS, Chiu HF, Tse LK, Woo KS. Obstructive sleep apnea presenting with nocturnal angina, heart failure, and near-miss sudden death. Chest. 1991 Apr;99(4):1023-5.
45. Gami AS, Hodge DO, Herges RM, Olson EJ, Nykodem J, Kara T, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. J Am Coll Cardiol. 2007 Feb 6;49(5):565-71.
46. Martinez-Garcia MA, Soler-Cataluna JJ, Roman-Sanchez P, Gonzalez V, Amoros C, Montserrat JM. Obstructive sleep apnea has little impact on quality of life in the elderly. Sleep Med. 2009 Jan;10(1):104-11.
47. Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. JAMA. 2004 Apr 28;291(16):2013-6.
48. Enright PL, Newman AB, Wahl PW, Manolio TA, Haponik EF, Boyle PJ. Prevalence and correlates of snoring and observed apneas in 5,201 older adults. Sleep. 1996 Sep;19(7):531-8.
49. O'Connor GT, Lind BK, Lee ET, Nieto FJ, Redline S, Samet JM, et al. Variation in symptoms of sleep-disordered breathing with race and ethnicity: the Sleep Heart Health Study. Sleep. 2003 Feb 1;26(1):74-9.
50. Cherniack EP, Cherniack NS. Obstructive sleep apnea, metabolic syndrome, and age: will geriatricians be caught asleep on the job? Aging Clin Exp Res. 2010 Feb;22(1):1-7.
51. Wang L, Li J, Xie Y, Zhang XG. Association between serum homocysteine and oxidative stress in elderly patients with obstructive sleep apnea/hypopnea syndrome. Biomed Environ Sci. 2010 Feb;23(1):42-7.
52. Zhuo SQ, Yang XP, Chen YC, Tian XT, Lian H, Ou Q. [Effect of obstructive sleep apnea syndrome on blood lipid and blood glucose in elderly hypertensive patients]. Nan Fang Yi Ke Da Xue Xue Bao. 2009 Feb;29(2):330-2.
53. Collop NA. The significance of sleep-disordered breathing and obstructive sleep apnea in the elderly. Chest. 1997 Oct;112(4):867-8.
54. Launois SH, Pepin JL, Levy P. Sleep apnea in the elderly: a specific entity? Sleep Med Rev. 2007 Apr;11(2):87-97.
55. Chung S, Yoon IY, Shin YK, Lee CH, Kim JW, Ahn HJ. Endothelial dysfunction and inflammatory reactions of elderly and middle-aged men with obstructive sleep apnea syndrome. Sleep Breath. 2009 Mar;13(1):11-7.
56. Wang Y, Li Y. [Clinical and polysomnographic characteristics in elderly patients with obstructive sleep apnea hypopnea syndrome]. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2008 Mar;22(5):222-5.
57. Teramoto S, Yamaguchi Y, Yamamoto H, Hanaoka Y, Ishii M, Shinichiro H, et al. Increase in oxidative stress levels in elderly patients with obstructive sleep apnea syndrome: effects of age and sex. J Am Geriatr Soc. 2008 Mar;56(3):569-71.
58. Endeshaw YW, Katz S, Ouslander JG, Blilwise DL. Association of denture use with sleep-disordered breathing among older adults. J Public Health Dent. 2004 Summer;64(3):181-3.
59. Kobayashi M, Namba K, Tsuiki S, Matsuo A, Sugiura T, Inoue Y. Clinical characteristics in two subgroups of obstructive sleep apnea syndrome in the elderly-comparison between cases with elderly and middle-age onset. Chest. 2010 Apr 2.
60. Bombois S, Derambure P, Pasquier F, Monaca C. Sleep disorders in aging and dementia. J Nutr Health Aging. 2010;14(3):212-7.
61. Rakel RE. Clinical and societal consequences of obstructive sleep apnea and excessive daytime sleepiness. Postgrad Med. 2009 Jan;121(1):86-95.
62. Archbold KH, Borghesani PR, Mahurin RK, Kapur VK, Landis CA. Neural activation patterns during working memory tasks and OSA disease severity: preliminary findings. J Clin Sleep Med. 2009 Feb 15;5(1):21-7.
63. Mazza S, Pepin JL, Naegele B, Plante J, Deschaux C, Levy P. Most obstructive sleep apnoea patients exhibit vigilance and attention deficits on an extended battery of tests. Eur Respir J. 2005 Jan;25(1):75-80.
64. Bedard MA, Montplaisir J, Richer F, Rouleau I, Malo J. Obstructive sleep apnea syndrome: pathogenesis of neuropsychological deficits. J Clin Exp Neuropsychol. 1991 Nov;13(6):950-64.
65. Onen F, Higgins S, Onen SH. Falling-asleep-related injured falls in the elderly. J Am Med Dir Assoc. 2009 Mar;10(3):207-10.
66. Aguiar M, Valenca J, Felizardo M, Caeiro F, Moreira S, Staats R, et al. Obstructive sleep apnoea syndrome as a cause of road traffic accidents. Rev Port Pneumol. 2009 May-Jun;15(3):419-31.
67. Mulgrew AT, Nasvadi G, Butt A, Cheema R, Fox N, Fleetham JA, et al. Risk and severity of motor vehicle crashes in patients with obstructive sleep apnoea/hypopnoea. Thorax. 2008 Jun;63(6):536-41.
68. Abdal H, Pizzimenti JJ, Purvis CC. The eye in sleep apnea syndrome. Sleep Med. 2006 Mar;7(2):107-15.
69. Palombi K, Renard E, Levy P, Chiquet C, Deschaux C, Romanet JP, et al. Non-arteritic anterior ischaemic optic neuropathy is nearly systematically associated with obstructive sleep apnoea. Br J Ophthalmol. 2006 Jul;90(7):879-82.
70. Andersen ML, Santos-Silva R, Bittencourt LR, Tufik S. Prevalence of erectile dysfunction complaints associated with sleep disturbances in Sao Paulo, Brazil: A population-based survey. Sleep Med. 2010 Apr 26.
71. Malhotra A, Huang Y, Fogel R, Lazic S, Pillar G, Jakab M, et al. Aging influences on pharyngeal anatomy and physiology: the predisposition to pharyngeal collapse. Am J Med. 2006 Jan;119(1):72 e9-14.
72. Malhotra A, Huang Y, Fogel RB, Pillar G, Edwards JK, Kikinis R, et al. The male predisposition to pharyngeal collapse: importance of airway length. Am J Respir Crit Care Med. 2002 Nov 15;166(10):1388-95.
73. Thurnheer R, Wraith PK, Douglas NJ. Influence of age and gender on upper airway resistance in NREM and REM sleep. J Appl Physiol. 2001 Mar;90(3):981-8.
74. Worsnop C, Kay A, Kim Y, Trinder J, Pierce R. Effect of age on sleep onset-related changes in respiratory pump and upper airway muscle function. J Appl Physiol. 2000 May;88(5):1831-9.
75. Browne HA, Adams L, Simonds AK, Morrell MJ.

- Ageing does not influence the sleep-related decrease in the hypercapnic ventilatory response. *Eur Respir J.* 2003 Mar;21(3):523-9.
76. Martin SE, Mathur R, Marshall I, Douglas NJ. The effect of age, sex, obesity and posture on upper airway size. *Eur Respir J.* 1997 Sep;10(9):2087-90.
77. Enciso R, Nguyen M, Shigeta Y, Ogawa T, Clark GT. Comparison of cone-beam CT parameters and sleep questionnaires in sleep apnea patients and control subjects. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2010 Feb;109(2):285-93.
78. Ando E, Ogawa T, Shigeta Y, Hirai S, Ikawa T, Ishikawa C, et al. A case of obstructive sleep apnoea with anterior cervical osteophytes. *J Oral Rehabil.* 2009 Oct;36(10):776-80.
79. Beneto A, Gomez-Siurana E, Rubio-Sanchez P. Comorbidity between sleep apnea and insomnia. *Sleep Med Rev.* 2009 Aug;13(4):287-93.
80. Ayalon L, Ancoli-Israel S, Aka AA, McKenna BS, Drummond SP. Relationship between obstructive sleep apnea severity and brain activation during a sustained attention task. *Sleep.* 2009 Mar 1;32(3):373-81.
81. Yaouhi K, Bertran F, Clochon P, Mezenge F, Denise P, Foret J, et al. A combined neuropsychological and brain imaging study of obstructive sleep apnea. *J Sleep Res.* 2009 Mar;18(1):36-48.
82. Meek D, Chakravorty I. Obstructive sleep apnoea increases risk of CVD. *Practitioner.* 2009 Nov;253(1723):17-20, 2.
83. Tiihonen P, Hukkanen T, Tuomilehto H, Mervaala E, Toyras J. Evaluation of a novel ambulatory device for screening of sleep apnea. *Telemed J E Health.* 2009 Apr;15(3):283-9.
84. Tiihonen P, Hukkanen T, Tuomilehto H, Mervaala E, Paakkonen A, Toyras J. Accuracy of automatic analysis of ambulatory recordings of nocturnal breathing disorders is significantly instrumentation dependent. *J Med Eng Technol.* 2009;33(5):386-93.
85. Onen F, Onen SH. Fundamentals of quality of life and daytime sleepiness measurements in older sleep apnea patients. *Sleep Med.* 2010 Mar;11(3):332; author reply -3.
86. Valdivia-Arenas MA, Powers M, Khayat RN. Sleep-disordered breathing in patients with decompensated heart failure. *Heart Fail Rev.* 2009 Sep;14(3):183-93.
87. Ancoli-Israel S, Coy T. Are breathing disturbances in elderly equivalent to sleep apnea syndrome? *Sleep.* 1994 Feb;17(1):77-83.
88. Blilwise DL, Blilwise NG, Partinen M, Pursley AM, Dement WC. Sleep apnea and mortality in an aged cohort. *Am J Public Health.* 1988 May;78(5):544-7.
89. Bixler EO, Vgontzas AN, Ten Have T, Tyson K, Kales A. Effects of age on sleep apnea in men: I. Prevalence and severity. *Am J Respir Crit Care Med.* 1998 Jan;157(1):144-8.
90. Onen SH, Dubray C, Decullier E, Moreau T, Chapuis F, Onen F. Observation-based nocturnal sleep inventory: screening tool for sleep apnea in elderly people. *J Am Geriatr Soc.* 2008 Oct;56(10):1920-5.
91. Pagel JF. The burden of obstructive sleep apnea and associated excessive sleepiness. *J Fam Pract.* 2008 Aug;57(8 Suppl):S3-8.
92. Takama N, Kurabayashi M. Effectiveness of a portable device and the need for treatment of mild-to-moderate obstructive sleep-disordered breathing in patients with cardiovascular disease. *J Cardiol.* 2010 Apr 8.
93. Oktay B, Akbal E, Firat H, Ardic S, Kizilgun M. CPAP treatment in the coexistence of obstructive sleep apnea syndrome and metabolic syndrome, results of one year follow up. *Acta Clin Belg.* 2009 Jul-Aug;64(4):329-34.
94. Martinez-Garcia MA, Soler-Cataluna JJ, Ejarque-Martinez L, Soriano Y, Roman-Sanchez P, Illa FB, 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 Jul 1;180(1):36-41.
95. Middleton S, Vermeulen W, Byth K, Sullivan CE, Middleton PG. Treatment of obstructive sleep apnoea in Samoa progressively reduces daytime blood pressure over 6 months. *Respirology.* 2009 Apr;14(3):404-10.
96. Machado MC, Vollmer WM, Togeiro SM, Bilderback AL, Oliveira MV, Leitao FS, et al. CPAP and survival in moderate-to-severe obstructive sleep apnoea syndrome and hypoxaemic COPD. *Eur Respir J.* 2010 Jan;35(1):132-7.
97. Taskin U, Yigit O, Acioglu E, Aricigil M, Toktas G, Guzelhan Y. Erectile dysfunction in severe sleep apnea patients and response to CPAP. *Int J Impot Res.* 2010 Mar;22(2):134-9.
98. Ribeiro Franco CM, Cestaro Bonanni J, Jaguaribe AM, Ataide L, Jr. Study into the use of continuous positive airway pressure in obstructive sleep apnoea-hypopnoea syndrome patients with daytime drowsiness. *Rev Port Pneumol.* 2009 Mar-Apr;15(2):215-26.
99. Garvey JF, McNicholas WT. Continuous positive airway pressure therapy: new generations. *Indian J Med Res.* 2010 Feb;131:259-66.
100. Bardwell WA, Ancoli-Israel S, Berry CC, Dimsdale JE. Neuropsychological effects of one-week continuous positive airway pressure treatment in patients with obstructive sleep apnea: a placebo-controlled study. *Psychosom Med.* 2001 Jul-Aug;63(4):579-84.
101. Lim W, Bardwell WA, Loredo JS, Kim EJ, Ancoli-Israel S, Morgan EE, et al. Neuropsychological effects of 2-week continuous positive airway pressure treatment and supplemental oxygen in patients with obstructive sleep apnea: a randomized placebo-controlled study. *J Clin Sleep Med.* 2007 Jun 15;3(4):380-6.
102. Sanchez AI, Martinez P, Miro E, Bardwell WA, Buela-Casal G. CPAP and behavioral therapies in patients with obstructive sleep apnea: effects on daytime sleepiness, mood, and cognitive function. *Sleep Med Rev.* 2009 Jun;13(3):223-33.
103. Sassani A, Findley LJ, Kryger M, Goldlust E, George C, Davidson TM. Reducing motor-vehicle collisions, costs, and fatalities by treating obstructive sleep apnea syndrome. *Sleep.* 2004 May 1;27(3):453-8.
104. Horstmann S, Hess CW, Bassetti C, Gugger M, Mathis J. Sleepiness-related accidents in sleep apnea patients. *Sleep.* 2000 May 1;23(3):383-9.
105. Tan MC, Ayas NT, Mulgrew A, Cortes L, FitzGerald JM, Fleetham JA, et al. Cost-effectiveness of continuous positive airway pressure therapy in patients with obstructive sleep apnea-hypopnea in British Columbia. *Can Respir J.* 2008 Apr;15(3):159-65.
106. Mazza S, Pepin JL, Naegele B, Rauch E, Deschaux C, Ficheux P, et al. Driving ability in sleep apnoea patients before and after CPAP treatment: evaluation on a road safety platform. *Eur Respir J.* 2006 Nov;28(5):1020-8.
107. Cooke JR, Ayalon L, Palmer BW, Loredo JS, Corey-Bloom J, Natarajan L, et al. Sustained use of CPAP slows deterioration of cognition, sleep, and mood in patients with Alzheimer's disease and obstructive sleep apnea: a preliminary study. *J Clin Sleep Med.* 2009 Aug 15;5(4):305-9.
108. Ancoli-Israel S, Palmer BW, Cooke JR, Corey-Bloom J, Fiorentino L, Natarajan L, et al. Cognitive effects of treating obstructive sleep apnea in Alzheimer's disease: a

- randomized controlled study. *J Am Geriatr Soc.* 2008 Nov;56(11):2076-81.
109. Holty JE, Guilleminault C. Surgical options for the treatment of obstructive sleep apnea. *Med Clin North Am.* 2010 May;94(3):479-515.
110. Powell NB. Contemporary surgery for obstructive sleep apnea syndrome. *Clin Exp Otorhinolaryngol.* 2009 Sep;2(3):107-14.
111. Lundkvist K, Januszewicz A, Friberg D. Uvulopalatopharyngoplasty in 158 OSAS patients failing non-surgical treatment. *Acta Otolaryngol.* 2009 Nov;129(11):1280-6.
112. AlGhanim N, Comondore VR, Fleetham J, Marra CA, Ayas NT. The economic impact of obstructive sleep apnea. *Lung.* 2008 Jan-Feb;186(1):7-12.
113. Selim B, Won C, Yaggi HK. Cardiovascular consequences of sleep apnea. *Clin Chest Med.* 2010 Jun;31(2):203-20.
114. Meng S, Fang L, Wang CQ, Wang LS, Chen MT, Huang XH. Impact of obstructive sleep apnoea on clinical characteristics and outcomes in patients with acute coronary syndrome following percutaneous coronary intervention. *J Int Med Res.* 2009 Sep-Oct;37(5):1343-53.
115. Hoffman B, Wingenbach DD, Kagey AN, Schaneman JL, Kasper D. The long-term health plan and disability cost benefit of obstructive sleep apnea treatment in a commercial motor vehicle driver population. *J Occup Environ Med.* 2010 May;52(5):473-7.
116. Duran-Cantolla J, Aizpuru F, Martinez-Null C, Barbe-Illa F. Obstructive sleep apnea/hypopnea and systemic hypertension. *Sleep Med Rev.* 2009 Oct;13(5):323-31.
117. Pack AI, Gislason T. Obstructive sleep apnea and cardiovascular disease: a perspective and future directions. *Prog Cardiovasc Dis.* 2009 Mar-Apr;51(5):434-51.
118. McDaid C, Griffin S, Weatherly H, Duree K, van der Burgt M, van Hout S, et al. Continuous positive airway pressure devices for the treatment of obstructive sleep apnoea-hypopnoea syndrome: a systematic review and economic analysis. *Health Technol Assess.* 2009 Jan;13(4):iii-iv, xi-xiv, 1-119, 43-274.
119. Ram S, Seirawan H, Kumar SK, Clark GT. Prevalence and impact of sleep disorders and sleep habits in the United States. *Sleep Breath.* 2010 Feb;14(1):63-70.
120. Blythe J, Doghramji PP, Jungquist CR, Landau MB, Valerio TD, Ancoli-Israel S, et al. Screening & treating patients with sleep/wake disorders. *JAAPA.* 2009 Dec;Suppl Sleep:1-17; quiz 9.
121. Culebras A. A review of frontiers in clinical sleep medicine. *Rev Neurol Dis.* 2010;7(1):9-18.

Author Information

Harsha Vardhan Ganga, MD, MPH

Clinical Assistant Professor (Adjunct), Internal Medicine Department University of Iowa, Carver College of Medicine, Iowa City Des Moines University School of Osteopathic Medicine, Des Moines Mercy Medical Center North Iowa, Mason City.

Yuvaraj Thangaraj, MD, FACSG

Clinical Assistant Professor (Adjunct), Internal Medicine Department University of Iowa, Carver College of Medicine, Iowa City Des Moines University School of Osteopathic Medicine, Des Moines Mercy Medical Center North Iowa, Mason City.

Venkat Puppala, MD, MPH

Internal Medicine Bay Area Medical Center Marinette, Wisconsin

Nandini Kolla, MD

Internal Medicine Residency Abington Memorial Hospital Philadelphia.