

Podcast of the *Journal of Clinical Sleep Medicine*

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Welcome to the regular podcast of the *Journal of Clinical Sleep Medicine*. I am Dr. Stuart Quan, editor of the *Journal*. These podcasts are a regular feature of each issue of the *Journal* and can be downloaded at the *Journal's* website. Each podcast features summaries of important articles published in the current issue of the *Journal*, as well as occasional interviews with authors of these papers.

The first paper to be discussed in this issue of the *Journal* is entitled, "Exercise Training Improves Selected Aspects Of Daytime Functioning In Adults With Obstructive Sleep Apnea," by Dr. Christopher E. Kline and colleagues from the University of Pittsburgh in Pittsburgh, PA and the University of South Carolina in Columbia, SC. Several epidemiologic studies have demonstrated that individuals who exercise regularly appear to have a decrease in sleep apnea severity in comparison to those who do not engage in regular exercise. In addition, small clinical studies have shown that intervention with a regular exercise program, even in the absence of weight loss, results in a decrease in sleep apnea severity. In this study, 43 sedentary and overweight adults between the ages of 18 and 55 years with sleep apnea severity of at least an apnea-hypopnea index greater than or equal to 15 were randomized to either 12 weeks of moderate-intensity aerobic and resistance exercise training or a control group consisting of low-intensity stretching. Single night laboratory polysomnography was performed before starting the program and afterwards. In addition, questionnaire-based measures of mood, daytime sleepiness, and quality of life were administered before and after the program, as well as a neurobehavioral performance battery. There were 27 subjects assigned to the exercise-training arm of the study and 16 assigned to the control arm.

At baseline, the apnea-hypopnea index of the exercise-training arm was 32.2 and that for the control arm was 24.4. After completion of the program, the apnea-hypopnea index in the exercise-training arm declined significantly to 24.5 but there was no significant change in the control arm, with the apnea-hypopnea index equal to 28.9. In comparison to the control arm, exercise training improved mood, as demonstrated by a decrease in the Center for Epidemiologic Studies Depression Scale, and the fatigue subscale of the Profile of Moods States questionnaire. In addition, the vigor subscale of the Profile of Moods States questionnaire increased. No changes were observed in the control arm. With respect to quality of life, the physical functioning, vitality and mental health subscales of the SF36 improved following exercise training and there was no significant change in the control arm. In contrast, exercise

training did not have any effect on any of the instruments of the neurobehavioral test battery.

The authors conclude that exercise training produced moderate improvements in some aspects of daytime functioning in patients with moderately severe obstructive sleep apnea. They caution, however, that this was a small trial and that additional studies with larger numbers of participants are needed.

The next study to be summarized in this podcast is entitled, "Smoking Induces Oropharyngeal Narrowing and Increases the Severity Of Obstructive Sleep Apnea Syndrome," by Dr. Kyung Soo Kim and colleagues from Chung-Ang University in Seoul, Korea, and the Yonsei Snoring Clinic in Seongnam, Gyeonggi-Do, Korea. Several studies have demonstrated that cigarette smoking appears to be a risk factor for either sleep apnea or snoring. However, there have been relatively few studies that have investigated the severity of sleep apnea in association with histological changes in the upper airway. In this study, the records of 122 patients who had undergone a uvulopalatopharyngoplasty between March, 2005, and February, 2008, for obstructive sleep apnea were reviewed. 57 male patients with a well-documented smoking history, normal cephalometrics except for a narrowed oral pharynx and available tissue from their uvular specimens were selected. The patients were classified as having mild, moderate or severe obstructive sleep apnea based on polysomnography. Definitions were mild disease, with an apnea-hypopnea index between 5-15, moderate between 15-30 and severe greater than 30. Smoking history was categorized as non-smoking or smoking. In addition, smokers were subdivided into those with a less than a 10-pack year history and those with a greater than a 10-pack year history.

The authors found that, in general, non-smokers had less severe obstructive sleep apnea than smokers. The apnea-hypopnea index of non-smokers was 22.35 and for smokers was 30.32. When stratified by smoking history, smokers with less than a 10-pack year history had an apnea-hypopnea index of 25.22 versus 34.14 for smokers who had a greater than 10-pack year history. In addition, more smokers than non-smokers fell into the moderate to severe obstructive sleep apnea categories. When the histologic changes observed in the uvular mucosa were compared among mild, moderate and severe smokers, it was observed that smokers had a greater thickness of their lamina propria. In addition, when the smokers were stratified by severity of sleep apnea, the thickness of the lamina propria increased progressively from mild through severe obstructive sleep apnea. The epithelium of the smokers was characterized by increased amounts of edema. The authors also performed

immuno-histochemical staining for Protein Gene Product 9.5, Substance P and calcitonin gene-related peptide to determine the expression of peripheral sensory nerves in the uvular specimens. They found that there were no differences between smokers and non-smokers in staining for Substance P or for Protein Gene Product 9.5. However, smokers had greater expression of calcitonin gene-related protein than non-smokers. Furthermore, smokers smoked greater than 10 pack years had higher values of calcitonin gene-related protein than those who smoked lesser amounts

The authors conclude that smoking produces thickened or edematous uvular mucosa, which is mediated by calcitonin gene-related protein induced neurogenic inflammation. This process contributes to upper airway narrowing in individuals with obstructive sleep apnea. Thus, this may be the mechanism by which smoking is a risk factor for obstructive sleep apnea.

The final paper to be discussed in this podcast is entitled, "Restless Nocturnal Eating: A Common Feature Of Willis-Ekbom Syndrome (RLS)," by Drs. Michael Howell and Carlos Schenck from the University of Minnesota in Minneapolis, MN. Restless-leg syndrome is characterized by uncomfortable sensations, primarily in the lower extremities, when an individual is at rest and compels the afflicted person to move their lower extremities to obtain relief. Consequently, many individuals with restless-leg syndrome have difficulty with initiating sleep at night and, as a consequence, have impairment in daytime functioning. Recent studies have observed an association between sleep-related eating disorder and restless-leg syndrome. However, it is unclear whether the nocturnal eating is related to the underlying pathophysiology of restless-leg syndrome, or is a behavioral manifestation of increased time spent awake by restless-leg syndrome patients. In this study, 88 patients with restless-leg syndrome and 42 patients with psychophysiologic insomnia completed a structured, one-page, nocturnal-eating questionnaire. Individuals were considered to have nocturnal eating if they admitted to doing so at least once per month. Sleep-related eating disorder was considered present if the nocturnal eating was associated with ingestion of unusual or inedible substances, difficulty falling back to sleep or non-restorative sleep, sleep-related injury or potentially injurious behaviors, morning anorexia or other adverse health consequences. Patients in both groups were then followed prospectively. The authors found that nocturnal eating was present in 61% of restless-leg patients and only 12% of insomnia patients. In addition, sleep-related eating disorder was present in 36% of restless-leg patients versus zero percent in insomnia patients. Amnesic sleep-related eating disorder, or sleep walking, was more likely to occur in restless-leg patients who were treated with sedative hypnotics in comparison to insomnia patients who were treated with sedative hypnotics. 44 of the restless-leg syndrome patients had information concerning pharmacologic treatment. After treatment with dopaminergic agents, with an average duration of follow up of 11.8 months, both nocturnal

eating and sleep-related eating disorder among the restless-leg patients declined by 50%. The authors conclude that nocturnal eating is a frequent manifestation of restless-leg syndrome and that inappropriate treatment of restless-leg syndrome patients with sedative hypnotics leads to drug-induced sleep-related eating disorder. In addition, they speculate that restless-leg syndrome may be a link between sleep-related eating disorder and night-eating syndrome. The latter condition is characterized by consumption of at least 25% of the daily food intake after the evening meal, with at least two episodes of nocturnal eating per week with clinical consequences.

I would also like to call the listeners attention to several other articles published in this issue of the *Journal*. In the "Analysis & Perspective" section of the *Journal*, Dr. Matt Bianchi and colleagues from Harvard Medical School in Boston, MA, critique the recent paper published by Kripke and colleagues linking use of hypnotics with mortality or cancer published this year in *BMJ Open*. This latter study reported a 3.5-5.5 times higher mortality in the hypnotic group than the control group. Dr. Bianchi and colleagues point out that there may be some significant methodological issues with the Kripke, et al., paper and call into question its conclusions. Also in this section of the *Journal*, Dr. Daniel F. Kripke and colleagues offers a response to the critique by Dr. Bianchi and colleagues concerning their paper in *BMJ Open*. They defend their analysis and maintain that a relationship between hypnotic use and mortality does exist. They also indicate that there is a need for randomized, clinical trials to explore long-term hypnotic safety. In the "Review" article section of the *Journal*, I would like to call the listener's attention to a paper by Dr. Mashaal Alshaikh from King Saad University, Riyadh, Saudi Arabia, St. Michael's Hospital, Toronto, Ontario, Canada and the University of Toronto in Toronto, Ontario, Canada, entitled, "Sodium Oxybate For Narcolepsy With Cataplexy: Systematic Review And Analysis." This paper was a meta-analysis of the safety and efficacy of sodium oxybate to treat narcolepsy. The authors found that sodium oxybate was efficacious in reducing cataplexy and daytime sleepiness and was relatively well tolerated with most adverse events being mild to moderate in severity.

Finally, the *Journal* received its first impact factor from Thomson ISI. It was 3.232, ranking the *Journal* as third among the seven non-review sleep journals who received impact factors. While as editor, I am proud to have received a relatively high impact factor for the *Journal*, I would like to remind the reader that the *Journal's* primary mission is to serve the educational and professional needs of the membership of the American Academy of Sleep Medicine and it will continue to publish articles of clinical relevance to them.

This concludes the regular podcast of the *Journal of Clinical Sleep Medicine*. The listener is encouraged to read the contents of the *Journal* for additional information regarding each of the articles summarized in this podcast, as well as other papers published in this issue of the *Journal*.