Obstructive sleep apnea is associated with an increased risk of colorectal neoplasia

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Background and Aims: A recent meta-analysis showed that obstructive sleep apnea (OSA) is associated with a higher prevalence of cancer and cancer-related mortality; however, little information is available on the association between OSA and colorectal neoplasia.

Methods: We identified consecutive patients who underwent overnight polysomnography (PSG) and subsequent colonoscopy. We compared the prevalence of colorectal neoplasia between patients with or without OSA according to the results of PSG. For each patient with OSA, 1 or 2 controls matched for age (±5 years), sex, body mass index (BMI), and smoking who had undergone first-time screening colonoscopy were selected.

Results: Of the 163 patients, 111 patients were diagnosed with OSA and 52 patients were within the normal range of the Apnea-Hypopnea Index. Of the 111 patients with OSA, 18 patients (16.2%) had advanced colorectal neoplasia, including 4 (3.6%) colorectal cancers. In the multivariate analyses, OSA was associated with an increased risk of advanced colorectal neoplasia after adjusting for factors including age and sex (mild: odds ratio [OR], 14.09; 95% confidence interval [CI], 1.55–127.83; $P = .019$; moderate or severe: OR, 14.12; 95% CI, 1.52–131.25; $P = .020$). Our case-control study revealed that the odds of detecting advanced colorectal neoplasia among patients with OSA were approximately 3.03 times greater than in the controls matched for age, sex, BMI, and smoking (OR, 3.03; 95% CI, 1.44–6.34; $P = .002$).

Conclusion: Physicians should be aware of the association between OSA and the development of colorectal neoplasia and explain the need for colonoscopy to patients with OSA. (Gastrointest Endosc 2017;85:568-73.)

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer worldwide and the fourth most common cause of cancer-related death.[1,2] Colorectal neoplasia, including cancer, is very common in people who live in industrialized countries.[1,3,4] More importantly, the incidence of CRC has increased rapidly in the last 10 years, including in Korea.[5] Adenomatous colorectal polyps are benign tumors of neoplastic epithelium with variable potential for malignancy.[6] It has been reported that the probability of carcinomatous transformation increases with polyp size, especially when the polyps are larger than 1 cm, have a villous component, or show a high degree of dysplasia.[6] Therefore, the detection and curative resection of advanced colorectal adenomatous polyps is very

Abbreviations: AHI, Apnea-Hypopnea Index; BMI, body mass index; CI, confidence interval; CRC, colorectal cancer; OR, odds ratio; OSA, obstructive sleep apnea; PSG, polysomnography; VAT, visceral adipose tissue.

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important to prevent CRC and to reduce CRC-related mortality.[7,8]

Obstructive sleep apnea (OSA) is a common disorder affecting at least 2% to 4% of the adult population.[9] OSA is the most common type of sleep-disordered breathing and is characterized by recurrent episodes of upper airway collapse during sleep. It is well known that OSA is an independent risk factor for cardiovascular disease, cerebrovascular disease, and metabolic disease.[10-18] A recent meta-analysis showed that patients with OSA have a higher prevalence of cancer and cancer-related mortality.[17] Of interest, some studies have demonstrated that colon cancer development may be associated with sleep apnea and hypoxic environments.[17,19] These data suggest a link between tumorigenesis in the colon and OSA. However, the association between OSA and colorectal neoplasia has not been investigated.

We studied patients who underwent standard polysomnography (PSG) and colonoscopy to investigate whether OSA is associated with an increased risk for colorectal neoplasia, including advanced neoplasia.

METHODS

Patients and data collection

This study was approved by the Institutional Review Board of Seoul National University Hospital and Seoul National University Boramae Hospital. We identified consecutive patients who underwent PSG and subsequent colonoscopy between January 2000 and March 2015. We classified these patients into non-OSA controls and patients with OSA according to the results of the PSG examination. Patients who underwent colonoscopy because of gastrointestinal bleeding, bowel habit changes, or a positive fecal occult blood test within the preceding month were excluded. We excluded patients with a previous history of colorectal cancer, inflammatory bowel disease, major colorectal surgery, and more than one first-degree relative with colorectal cancer. We also excluded patients who had undergone colonoscopy or sigmoidoscopy within the preceding 5 years.

Clinical information was obtained using the electronic medical recording system. The following data were included: age, sex, body mass index (BMI; kg/m^2), smoking (never smoker/ex-smoker/current smoker), alcohol consumption (men $\geq$60 g/day; women $\geq$40 g/day), and underlying diseases such as diabetes or hypertension.

Polysomnography

PSG was recorded with Twin-PSG software (Natus Neurology, West Warwick, RI) using a 6-channel electroencephalogram, a 4-channel electrooculogram, electromyogram, and electrocardiogram. A thermistor, a nasal air pressure monitoring sensor, an oximeter, piezoelectric bands, and a body position sensor were also applied to each patient. All patients complaining of snoring, arousal, or daytime sleepiness underwent PSG. The PSG results were interpreted by a board-certified neurologist or a psychiatrist who specialized in sleep disorders. OSA was defined as a reduction in airflow by 90% or more lasting 10 seconds or more.[20-23] Hypopnea was defined as a reduction in airflow by 30% or more lasting 10 seconds or more and accompanied by 4% or greater oxygen desaturation compared with a pre-event baseline.[24] The Apnea-Hypopnea Index (AHI) was used to grade the degree of severity of OSA. AHI <5 (events/h) was considered normal, $5 \leq$ AHI $<$ 15 was considered mild, $15 \leq$ AHI $<$ 30 was considered moderate, and AHI $\geq$30 was considered severe.[23,24]

Colonoscopy

Colonoscopy was performed by board-certified gastroenterologists using CF-240L and CF-H260 colonoscopes (Olympus, Tokyo, Japan). All procedures achieved the status of a complete examination. An examination was defined as complete when (1) the appendiceal orifice and ileocecal valve could be identified, (2) colonoscope withdrawal took at least 7 minutes, and (3) bowel preparation was adequate to visualize a minimum of 90% of the mucosa. Biopsy was performed on all abnormal mucosal lesions or they were resected using EMR, if possible. The size of lesions was assessed using the width of biopsy forceps or was measured after resection or surgery.

Lesions larger than 1 cm, with a villous component, or a high degree of dysplasia were classified as advanced adenomas. Serrated adenomas of 1 cm or more were also classified as advanced adenomas.[25] Carcinoma in situ or intramucosal carcinoma was classified as high-grade adenoma.[26,27] Advanced neoplasia was defined as either advanced adenoma or invasive carcinoma. In cases of multiple lesions, the most advanced pathology was selected as the definitive lesion. Non-advanced adenoma was defined as an adenoma <10 mm in size with low-grade dysplastic changes with <25% villous components. Nonspecific inflammation or hyperplastic lesions were classified as normal.

Case-control study

We performed a case-control study to determine whether patients with OSA have an increased risk of advanced colorectal neoplasia compared with the general population. In this analysis, we attempted to measure the odds of advanced neoplasia in patients with OSA compared with the general population at average risk for CRC. Therefore, we selected those aged 40 to 75 years among patients with OSA. Subsequently, we identified 1 or more individuals matched for age ($\pm$5 years), sex, BMI ($\pm$5 kg/m^2), and smoking without snoring, pauses in breathing during sleep, or daytime sleepiness who underwent screening colonoscopy for the first time in our health promotion center. Those who underwent colonoscopy because of gastrointestinal bleeding, bowel habit changes, or a