

## Original Article

# The Frequency of Obstructive Sleep Apnea in Patients with Non-cystic Fibrosis Bronchiectasis

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**Cite this article as:** Borekci S, Sekibag Y, Musellim D. The frequency of obstructive sleep apnea in patients with non-cystic fibrosis bronchiectasis. *Turk Thorac J.* 2021; 22(4): 333-338.

## Abstract

**OBJECTIVE:** Interruption or reduction in airflow and desaturation is a theoretically expected result in bronchiectasis accompanied by excessive secretions in the airways, bronchial wall thickening, and destruction of the wall structure. The same mechanism of interruption or reduction in airflow and desaturation is valid for obstructive sleep apnea (OSA). However, data on the association of bronchiectasis with OSA are scarce. We aimed to investigate the frequency of OSA and related parameters in patients with non-cystic fibrosis bronchiectasis (NCFB).

**MATERIAL AND METHODS:** All 43 consecutive patients who presented to the outpatient clinic for bronchiectasis follow-up between January 1, 2018 and January 1, 2019 were included. The polysomnography (PSG) data of the 43 patients were reviewed. Groups of patients with and without OSA, as detected using PSG, were compared in terms of clinical, demographic, and polysomnographic parameters.

**RESULTS:** The mean age of the 43 patients was  $50 \pm 15$  years; 28 (65.2%) were female. OSA was detected in 24 (55.8%) of 43 patients, of whom 14 (32.6%) had mild, 5 (11.6%) had moderate, and 5 (11.6%) had severe OSA. Three (7.0%) patients were REM-dependent and 7 (16.3%) were position-dependent. When evaluated using logistic regression analysis, REM percentage (16.8% vs. 11.8%,  $P = .03$ ) and presence of witnessed apnea (33.3% vs. 15.7%,  $P = .01$ ) were observed to be significantly higher in the patients with OSA. The age factor was found at the significance limit ( $P = .05$ ).

**CONCLUSION:** The frequency of OSA in patients with NCFB is 55.8%. Investigating OSA using PSG is important in patients with NCFB, especially at advanced ages.

**KEYWORDS:** Non-cystic bronchiectasis, OSA, risk factors

**Received:** October 1, 2020

**Accepted:** February 12, 2021

## INTRODUCTION

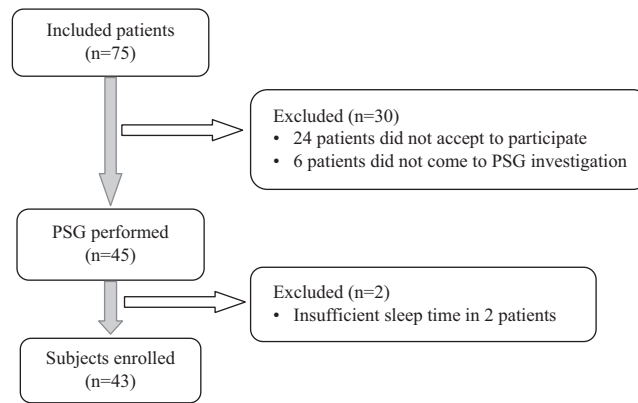
Interruption or reduction in airflow and desaturation is a theoretically expected result in bronchiectasis accompanied by excessive secretions in the airways, bronchial wall thickening, and destruction of the wall structure. The same mechanism of interruption or reduction in airflow and desaturation is valid for obstructive sleep apnea (OSA). However, data on the association of bronchiectasis with OSA are scarce.

OSA is characterized by recurrent partial or full airway obstruction resulting in hypoxia and arousals during sleep.<sup>1</sup> This condition, associated with increased cerebrovascular and cardiovascular mortality and morbidity rates, affects a substantial part of the population.<sup>2</sup> Studies have shown that the prevalence of OSA ranges between 23 and 50%.<sup>3</sup> OSA is a societal burden that increases direct and indirect costs by causing loss of labor force, in addition to altering the social life and quality of life of people because it is quite a common chronic condition.<sup>2</sup> However, OSA is a condition for which treatment is possible. Continuous positive airway pressure (CPAP) treatment is known to decrease mortality, morbidity, and other consequences of OSA.<sup>2</sup> In this regard, early diagnosis and treatment of a common condition like OSA are of great importance, both individually and socially.

Bronchiectasis is a chronic condition characterized by permanent dilation of the bronchi, accompanied by inflammatory changes in the bronchial walls and lung parenchyma adjacent to the bronchi.<sup>4</sup> Recurrent inflammation in the bronchus and fibrosis occurring in the parenchyma surrounding it are the fundamental basis of the pathogenesis of bronchiectasis.<sup>4</sup> Although the exact prevalence of bronchiectasis is unknown, an epidemiologic study in 2013 found that the prevalence of non-cystic fibrosis bronchiectasis (NCFB) was 139 per 100 000 capita after the age of 18, and that its prevalence increased prominently with age.<sup>5</sup> Being one of the obstructive airway diseases, but not investigated as much as asthma and chronic obstructive pulmonary disease (COPD), bronchiectasis currently has many unknown features.<sup>6,7</sup> The data about the association of bronchiectasis with OSA are very limited. Faria Junior et al.<sup>4</sup> reported that the prevalence of OSA in patients with non-cystic fibrosis was 40.82%.<sup>4</sup> In most of the studies, especially in those conducted before 2015, polysomnography (PSG) which is the gold-standard in the diagnosis of OSA, was not used.<sup>8-10</sup> In a study in 2015, hypoxemia,

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**Figure 1.** Flow chart.

as detected using PSG, was found to be related to indexes of life quality of patients with NCFB, and another study in 2017 linked PSG results to several parameters such as the colonization of sputum, number of attacks, and respiratory function tests.<sup>4,11</sup>

In the present study, we aimed to investigate the frequency of OSA and the parameters related to this in patients with NCFB.

## MATERIAL AND METHODS

The present study included the patients presenting to the outpatient clinic for bronchiectasis of the Respiratory Diseases Department of our university between January 1, 2018, and January 1, 2019. High-resolution computed tomography (HRCT) was used in making the diagnosis of bronchiectasis.<sup>12</sup> In all patients, the presence and extent of bronchiectasis were reported by a radiologist based on the guiding criteria of the British Thoracic Society for bronchiectasis in adult patients.<sup>13</sup> The study included patients who had a negative cystic fibrosis sweat test (chloride concentration < 30 mmol or negative cystic fibrosis transmembrane conductance gene analysis) and patients aged 18 years or over.<sup>14</sup> Patients with a diagnosis of cystic fibrosis, those who had an infectious attack in the last 1 month, those using an oxygen concentrator or a non-invasive mechanical ventilator, and those with co-morbidities that might be risky for OSA such as hypothyroidism, asthma, COPD, malignancy, or cardiac failure, were excluded.

The study was approved by the local Ethics Committee (Approval number: 23786442-604.01.01-102359) and written informed consent was taken from all participants.

It was planned to include all of the volunteer consecutive patients who presented to the outpatient clinic for bronchiectasis follow-up between January 1, 2018, and January 1, 2019, and met the inclusion criteria. Seventy-five patients were included, demographic and anthropometric characteristics of the patients in the study were recorded, and their essential OSA symptoms were enquired (snoring, witnessed apnea, excessive daytime sleepiness). They underwent a spirometric examination. The Epworth Sleepiness Scale was used. The status of sputum colonization was assessed. The extent and type of bronchiectasis were examined using HRCT. Twenty-four patients did not accept to participate in the study, and the PSG test was not available for 6 patients. A total of 45 patients underwent PSG in the sleep laboratory; 2 patients were excluded because sufficient sleep time was not achieved during PSG. A total of 43 patients were included in the final analysis (Figure 1).

## PSG

Overnight PSG recordings of the patients included in the study were made using the DOMINO software (version 2.5.0, Somnomedics). Two-channel electroencephalography (EEG) (EEG cables; C4-A1, C3-A2), two-channel electro-oculography (EOG), electromyogram (EMG) both from the chin and the tibialis anterior, two-lead electrocardiography (ECG), respiratory sounds, oxygen saturation, as well as thoracic and abdominal respiratory movements were recorded. Synchronized video recording was also made using a body position detector and nasal pressure sensor. Abnormal respiratory events related to sleep were scored using epochs of 30 seconds based on the 2012 criteria of the American Academy of Sleep Medicine (AASM).<sup>15</sup> Apnea was defined as an interruption of the airflow for 10 seconds. In defining hypopnea, an accompaniment of a 30% decrease of flow to 3% desaturation was used. Using this definition of hypopnea, apnea and hypopnea indexes (AHI) per sleep-hour were estimated to define OSA. Patients with AHI  $\geq 5$  were considered as having OSA, and those with AHI of 5-14, 15-29, and  $\geq 30$  were classified as having mild, moderate, and severe OSA, respectively. REM-dependent OSA was described as AHI  $\geq 5$  and AHI < 5 during the non-REM period, and AHI during the REM period being twice as much as during the non-REM period.<sup>16</sup> Similarly, position-dependent OSA was described as AHI  $\geq 5$  and AHI < 5 in the supine position, and AHI in the supine position was more than twice as much as in the non-supine position.<sup>16,17</sup>

## MAIN POINTS

- The frequency of OSA in patients with non-cystic fibrosis bronchiectasis is 55.8%.
- The frequency of OSA in patients with non-cystic fibrosis bronchiectasis increases with age.
- Investigating OSA using PSG is important in patients with non-cystic fibrosis bronchiectasis, especially at advanced ages.

### Epworth Sleepiness Scale (ESS)

The ESS is a questionnaire consisting of 8 items, and is used to demonstrate daytime sleepiness status. The patient answers each question by giving points ranging from 0 to 3. This questionnaire enquires the possibility of sleeping in certain situations on an ordinary day during which the patient is not very tired. The enquiry method is the same for all questions, and 0 points are given if there is no possibility of sleeping, 1 point if the possibility of sleeping is of low, 2 points if there is an intermediate possibility of sleeping, and 3 points are given if there is a high possibility of sleeping in the daytime. A total score of 10 or more indicates excessive daytime sleepiness.<sup>1</sup> The Turkish version of the ESS has been validated.<sup>18</sup>

### Sputum Colonization

Sputum colonization was defined as the growth of the same pathogen bacteria in 3 sputum samples obtained with time intervals of at least 1 month in the last year.

### Respiratory Function Test

All patients underwent spirometric evaluation during the stable phase using a Sensor Medics Vmax device (SensorMedics Series 22, USA) in the pulmonary function laboratory of our university. Spirometry was performed according to the criteria of the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines.<sup>19</sup>

### Statistical Analysis

Statistical analyses were performed using statistical software (SPSS, version 10.0; SPSS Inc., Chicago, IL, USA). Mean and standard deviation (SD) were calculated for the variables with normal distribution, and medians were calculated for variables not showing normal distribution. Categorical variables were expressed as percentages. The Mann–Whitney U-test and chi-square tests were used to compare the groups, and Spearman's test for assessing correlations. The significance level was set at  $P < .05$ .

## RESULTS

The clinical, demographic, and anthropometric characteristics of the 43 patients included in the study and the findings related to bronchiectasis are given in Table 1.

Twenty-five (58.1%) of the patients were aged over 50 years. The duration of the disease was more than 30 years in 22 (51.2%) patients. Disease symptoms started before the age of 20 years in 20 (46.5%) patients. In the spirometry, an obstructive pattern was found in 29 (67%) patients, and a restrictive pattern was seen in 19 (44%) participants.

The mean ESS score was  $6.3 \pm 4.7$  in the patients. OSA was found in 24 (55.8%) patients. Of them, 14 (32.6%) had mild, 5 (11.6%) had moderate, and 5 (11.6%) had severe OSA. Three (7.0%) patients were REM-dependent and seven (16.3%) were position-dependent.

The PSG data of the patients are given in Table 2.

Eighty-six percent of the patients had at least one of the essential symptoms of OSA, with the most frequently reported symptom being daytime sleepiness at a rate of 74.4%. The rate of patients with both snoring and daytime sleepiness was

86%. Among the main complaints, only the presence of witnessed apnea was statistically significantly higher in patients with OSA (33.3% vs. 15.7%,  $P = .01$ ).

The features of the patients with and without OSA and their comparison are given in Table 3. A significant relationship of OSA was found with age ( $P = .01$ ), duration of disease

( $P = .03$ ), and percentage of REM sleep ( $P = .03$ ). The results of the analyses are given in Table 3.

A positive correlation of AHI with age ( $r = 0.51$ ,  $P = .01$ ) and duration of disease ( $r = 0.34$ ,  $P = .03$ ) was found in patients with bronchiectasis. When the factors found to be related to OSA in univariate analysis were examined, only the percentage of REM was significant ( $P = .03$ ). The factor of age remained at the significance limit ( $P = .05$ ). Significance disappeared for disease duration as for all other factors associated with bronchiectasis.

## DISCUSSION

In the present study, we found that the frequency of OSA in patients with bronchiectasis was 55.8% and related with age. In the study conducted by Junior et al.<sup>4</sup> in 2017, the prevalence of OSA in patients with non-cystic fibrosis was found as 40.82%, lower than in our study. Similar to our study, they found a high frequency of OSA compared with the normal population.<sup>4</sup> It has been reported in the literature that the prevalence of OSA increases with age.<sup>20</sup> Faria Junior et al.<sup>4</sup> found a significant relationship between age and the presence of OSA.<sup>4</sup> In our study, we found the same relationship at the limit of significance. Also, the positive correlation between AHI and age supports the opinion that there may be a relationship between age and the presence of OSA. Moreover, it has been emphasized that the prevalence of OSA increased after the age of 65 years; the mean age of patients with OSA was found as 58 years in our study, indicating that OSA may occur in this group of patients at earlier ages, as reported in the literature.<sup>4</sup>

In the HypnoLaus study published in 2015, the prevalence of OSA was reported as 23% in women and 50% in men.<sup>3</sup> The HypnoLaus study contains data about the general population, thus it can represent the OSA prevalence of the general population. In our study, OSA prevalence in patients with NCFB was reported as 55.8%. Considering the total prevalence of women and men in the HypnoLaus study, it can be said that OSA is more common in patients with NCFB. In the HypnoLaus study, the average AHI in patients aged between 40 and 60 years was 7.6, and the average AHI in those aged over 60 years was 14.3; a statistically significant difference was found between these groups.<sup>3</sup> Similarly, in our study, the prevalence of OSA increased with age. The percentage of REM sleep is 20–25% in the normal population, whereas we found that the duration of REM sleep decreased in patients with bronchiectasis (mean: 14.6%).<sup>21</sup> It is known that the duration of REM sleep decreases in patients with OSA.<sup>22</sup> In our study, the percentage of REM sleep, however, was statistically significantly higher in the OSA group than in the group without OSA (16.8% vs. 11.8%). We believe that further studies are

**Table 1.** Clinical, Demographic, and Anthropometric Features

Parameter	n = 43
Age (years) (mean ± SD)	50 ± 15
Male n (%)	15 (34.8)
Female n (%)	28 (65.2)
Age of onset (years) (mean ± SD)	21 ± 20
Duration of disease (years) (mean ± SD)	31 ± 19
BMI (kg/m <sup>2</sup> ) (mean ± SD)	26.2 ± 5.6
Essential symptoms n (%)	37 (86.0)
Snoring	30 (69.8)
Excessive daytime sleepiness	32 (74.4)
Witnessed apnea	11 (25.6)
Sputum colonization n (%)	16 (37.2)
<i>Pseudomonas aeruginosa</i>	10 (23.0)
<i>Candida albicans</i>	1 (2.0)
<i>Escherichia coli</i>	1 (2.0)
<i>Haemophilus influenzae</i>	2 (5.0)
<i>Pseudomonas alcaligenes</i>	1 (2.0)
<i>Klebsiella</i>	1 (2.0)
Brochiectasis localization n (%)	
Right upper lobe	17 (39.0)
Right middle lobe	19 (44.0)
Right lower lobe	24 (56.0)
Left upper lobe	12 (27.0)
Lingula	20 (46.0)
Left lower lobe	27 (62.0)
Type of bronchiectasis n (%)	
Cystic	12 (28.0)
Cylindrical	17 (40.0)
Varicose	7 (16.0)
Traction	5 (12.0)
Number of lobes with bronchiectasis n (mean ± SD)	2.3 ± 1.6
Spirometry	
FVC (%) (mean ± SD)	78.9 ± 20.0
FEV <sub>1</sub> (%) (mean ± SD)	64.5 ± 24.1
FEV <sub>1</sub> /FVC (%) (mean ± SD)	66.7 ± 13.9
FEV <sub>1</sub> /FVC < %75 n (%)	29 (67.4)

BMI, body mass index; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation.

warranted to interpret how this effect occurs, because there are many uncertainties about REM sleep.

Regarding sputum colonization in the present study, the most commonly found pathogen was *Pseudomonas aeruginosa* with a rate of 23%. This rate was similar to that of 20.6% found in 121 patients with NCFB in our clinic in 2016.<sup>23</sup> In the study by Faria Junior et al.,<sup>4</sup> a relationship was found

**Table 2.** Polysomnographic Parameters

AHI (mean ± SD)	13.8 ± 21.05 (median: 6.0)
Sleep duration (hours) (mean ± SD)	5.3 ± 1.1
Stage 1 (min) (mean ± SD)	21 ± 12
Stage 1 (%) (mean ± SD)	7.1 ± 4.6
Stage 2 (min) (mean ± SD)	185 ± 70
Stage 2 (%) (mean ± SD)	55.5 ± 14.1
Stage 3 (min) (mean ± SD)	65 ± 35
Stage 3 (%) (mean ± SD)	21.7 ± 12.3
REM (min) (mean ± SD)	46.7 ± 26.7
REM (%) (mean ± SD)	14.6 ± 7.5
Sleep efficiency (%) (mean ± SD)	71.7 ± 14.6
Apnea index (mean ± SD)	3.6 ± 11.9 (median: 0.5)
Hypopnea index (mean ± SD)	7.7 ± 8.9 (median: 4.5)
Maximum apnea duration (seconds) (mean ± SD)	16.9 ± 19.3 (median: 14)
Max hypopnea duration (seconds) (mean ± SD)	66.6 ± 37.8
Number of desaturations (n) (mean ± SD)	73 ± 130 (median: 34)
Minimum SaO <sub>2</sub> (%) (mean ± SD)	86.2 ± 7.5
SaO <sub>2</sub> under 90% (n) (mean ± SD)	47 ± 130 (median: 4)
SaO <sub>2</sub> under 80% (n) (mean ± SD)	10 ± 42 (median: 0)

AHI, apnea hypopnea index; min, minute; REM, rapid eye movement; SaO<sub>2</sub>, oxygen saturation; SD, standart deviation; sec, second.

between the colonization of *P. aeruginosa* and the presence of OSA; however, we found no relationship.<sup>4</sup>

Faria Junior et al.<sup>4</sup> measured daytime levels of sleepiness using the Berlin Scale and emphasized that it was more common compared with the normal population.<sup>4</sup> In our study, essential symptoms of OSA were enquired individually (snoring, witnessed apnea, excessive daytime sleepiness) and their relationship with OSA was examined. Among the main complaints in our study, only witnessed apnea was more common in patients with OSA. There was no significant difference in excessive daytime sleepiness and snoring. Based on this, we consider that it is important to evaluate patients at advanced ages for the presence of OSA regardless of whether the patient has symptoms.

In studies on patients with bronchiectasis, the relationship of spirometric values with several parameters has been reported. No significant relationship was found between quality of sleep and FEV<sub>1</sub>% in the study by Gao et al.<sup>24</sup> in 2014 on patients with bronchiectasis.<sup>24</sup> In a 2017 study by Faria Junior et al.,<sup>4</sup> a significant relationship of FEV<sub>1</sub>% was found with snoring time, oxygen desaturation index per hour, and peripheral oxygen saturation, but no significant

**Table 3.** Comparison of Patients with and Without OSA

	OSA (+)	OSA (-)	P
M/F	9/15	6/13	.76
Age (years) (mean $\pm$ SD)	58 $\pm$ 13	45 $\pm$ 15	.01
Duration of disease (years) (mean $\pm$ SD)	37.3 $\pm$ 19.8	23.7 $\pm$ 15.2	.03
BMI (kg/m <sup>2</sup> ) (mean $\pm$ SD)	26.8 $\pm$ 5.4	25.4 $\pm$ 5.9	.93
FVC (%) (mean $\pm$ SD)	78 $\pm$ 21	80 $\pm$ 19	.633
FEV <sub>1</sub> (%) (mean $\pm$ SD)	64 $\pm$ 26	65 $\pm$ 22	.760
FEV <sub>1</sub> /FVC (mean $\pm$ SD)	66 $\pm$ 14	67 $\pm$ 14	.816
Obstruction, n (%)	15 (62.5)	14 (73.7)	.523
Restriction, n (%)	11 (45.8)	8 (42.1)	1.000
Main complaints, n (%)	21 (87)	16 (84)	.3
Snoring	18(75)	12(63.1)	.82
Witnessed apnea	8(33.3)	3(15.7)	.01
Excessive daytime sleepiness	19(79.1)	13(68.4)	.33
Colonization, n (%)	11 (45.8)	5 (26.3)	.161
Bronchiectasis localization, n (%)			
Upper lobe	11 (45.8)	9 (47.4)	1.000
Lower lobe	14 (58.3)	15 (78.9)	.325
Number of lobes with bronchiectasis, n (mean $\pm$ SD)	2.3 $\pm$ 1.7	2.4 $\pm$ 1.3	.624
Type of bronchiectasis, n (%)			
Cystic	4 (16.6)	8 (42.1)	.08
Cylindrical	10 (41.6)	7 (36.8)	.96
Varicose	3 (13.0)	4 (21.0)	.51
Traction	4 (16.6)	1 (5.3)	.12
Epworth score (mean $\pm$ SD)	6.1 $\pm$ 4.9	6.6 $\pm$ 4.4	.50
Stage 1 (%) (mean $\pm$ SD)	7.8 $\pm$ 4.3	6.3 $\pm$ 4.8	.12
Stage 2 (%) (mean $\pm$ SD)	53.0 $\pm$ 12.0	58.6 $\pm$ 16.1	.31
Stage 3 (%) (mean $\pm$ SD)	22.2 $\pm$ 13.9	21.2 $\pm$ 10.4	.81
REM (%) (mean $\pm$ SD)	16.8 $\pm$ 8.5	11.8 $\pm$ 5.0	.03

BMI, body mass index; F, female; FVC, forced vital capacity; M, male; REM, rapid eye movement; SD, standard deviation.

relationship was found with other sleep parameters.<sup>4</sup> In our study, we found no significant relationship between the presence of OSA and spirometric parameters (FEV<sub>1</sub>, FVC, and FEV<sub>1</sub>/FVC).

In the available studies, no emphasis has been made on the relationship between the extent of bronchiectasis and the presence of OSA in patients with bronchiectasis. In our study, no significant relationship was found between the presence of OSA and the type and extent of bronchiectasis.

One of the limitations of the present study was that the study was a single-center study. However, patients with bronchiectasis from many cities of Turkey present to our center, which has been a specialized follow-up center for bronchiectasis since 1996. Thus, it may be considered that the patient population in the present study might have comprised a homogenous group to represent the general population of Turkey. Another limitation is the absence of a control group.

However, the results of studies conducted in the normal population were used while making comparisons.

Sleep disorders in patients with primary ciliary dyskinesia and cystic fibrosis have been assessed previously using several surveys and scales.<sup>9,10</sup> By contrast, our study included patients with NCFB in whom PSG was used, which is the gold-standard in the diagnosis of OSA, and this was used to make the diagnosis. This was one of the strengths of our study.

In conclusion, the frequency of OSA in patients with NCFB is 55.8% and increases with age. The relationship of OSA with REM sleep and the response of these patients to CPAP treatment is another unknown topic. Future studies on these topics will be guiding.

**Ethical Committee Approval:** This study was approved by Ethics committee of Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, (Approval No: 23786442-604.01.01-102359).

**Informed consent:** Written informed consent was obtained from the patients who agreed to take part in the study.

**Peer Review:** Externally peer-reviewed.

**Author Contributions:** Supervision - S.B., Y.S., B.M.; Design - S.B., Y.S., B.M.; Resources - S.B., Y.S., D.O.H.; Materials - S.B., Y.S., D.O.H., B.M.; Data Collection and/or Processing - S.B., Y.S., D.O.H.; Analysis and/or Interpretation - S.B., B.M.; Literature Search- S.B., Y.S., D.O.H.; Writing Manuscript - S.B., Y.S., D.O.H., B.M.; Critical Review - S.B., B.M.

**Conflict of interest:** The authors have no conflict of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

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