

# Obstructive Sleep Apnea Among Obese Patients With Type 2 Diabetes

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**OBJECTIVE**— To assess the risk factors for the presence and severity of obstructive sleep apnea (OSA) among obese patients with type 2 diabetes.

**RESEARCH DESIGN AND METHODS**— Unattended polysomnography was performed in 306 participants.

**RESULTS**— Over 86% of participants had OSA with an apnea-hypopnea index (AHI)  $\geq 5$  events/h. The mean AHI was  $20.5 \pm 16.8$  events/h. A total of 30.5% of the participants had moderate OSA ( $15 \leq \text{AHI} < 30$ ), and 22.6% had severe OSA ( $\text{AHI} \geq 30$ ). Waist circumference (odds ratio 1.1; 95% CI 1.0–1.1;  $P = 0.03$ ) was significantly related to the presence of OSA. Severe OSA was most likely in individuals with a higher BMI (odds ratio 1.1; 95% CI 1.0–1.2;  $P = 0.03$ ).

**CONCLUSIONS**— Physicians should be particularly cognizant of the likelihood of OSA in obese patients with type 2 diabetes, especially among individuals with higher waist circumference and BMI.

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**W**e report the prevalence of obstructive sleep apnea (OSA) and the factors that increase the risk and severity of OSA among 306 obese patients with type 2 diabetes enrolled in Sleep AHEAD, a four-site ancillary study of the Look AHEAD Trial (Action for Health in Diabetes).

**RESEARCH DESIGN AND METHODS**— Look AHEAD (1,2) is a 16-center trial investigating the long-term health impact of an intensive lifestyle intervention in 5,145 overweight and obese adults with type 2 diabetes. Exclusion criteria for Sleep AHEAD were previous treatment for OSA.

The protocol was approved by each site's Institutional Review Board. Participants interested in Sleep AHEAD were consented at a Look AHEAD screening visit. Efforts were made to enroll individuals with undiagnosed OSA using a symptom questionnaire (3). Because almost all of the first 80 participants had OSA upon polysomnography, the symptom screen was dropped as an eligibility criteria.

## Polysomnography

A home unattended overnight polysomnogram (Compumedics, Abbotsville, Australia) was performed using techniques developed for the Sleep Heart

Health Study except that airflow was measured by nasal pressure cannula and oronasal thermistor (4). Polysomnograms were scored using recommended criteria (5). Hypopneas had to be associated with a  $\geq 4\%$  oxygen desaturation (5). The overall failure rate for the home polysomnography recordings was 8%;  $>90\%$  were due to equipment breakdown.

Weight, height, waist (2), and neck (6) circumferences and the Epworth Sleepiness Scale (7) were assessed within 1 week of the polysomnogram without knowledge of its results.

## Statistical analysis

Participants were categorized by apnea-hypopnea index (AHI) into mild (5–14.9), moderate (15–29.9), and severe ( $\geq 30$ ) OSA. Group differences were assessed using  $\chi^2$  and  $t$  tests. Variables that were correlated with AHI were included in logistic regressions to predict the presence of OSA ( $\text{AHI} \geq 5$ ) and, after removing participants with no OSA ( $n = 40$ ), severity of OSA. The same variables were used to predict AHI as a continuous (log-transformed) variable. Interactions were included to assess sex differences. Research site was included in all models.

## RESULTS

### Participant characteristics

One participant with central sleep apnea was removed from all analyses. Participant characteristics are in Table 1. A total of 60% were women. Of the females, 90% were postmenopausal. Nearly three-quarters (72.0%) had dyslipidemia, 82.6% had hypertension, and 93.4% had the metabolic syndrome.

There were no differences between individuals who were enrolled in Sleep AHEAD ( $n = 305$ ) and those enrolled in Look AHEAD but not in Sleep AHEAD at the four Sleep AHEAD sites ( $n = 1,012$ ) in weight, BMI, sex, race/ethnicity, or waist circumference. Sleep AHEAD participants were slightly older ( $61.3 \pm 6.5$  vs.  $58.7 \pm 6.9$  years;  $P < 0.0001$ ) and had lower A1C values ( $7.2 \pm 1.1$  vs.  $7.4 \pm 1.2\%$ ;  $P = 0.03$ ) than Look AHEAD participants who were not enrolled in Sleep AHEAD. There were small but significant differences in the frequency of snoring

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Table 1—Sleep AHEAD participant characteristics at baseline

|   | Total Sleep AHEAD participants | Sleep AHEAD participants (male) | Sleep AHEAD participants (female) | P       |
|---|--------------------------------|---------------------------------|-----------------------------------|---------|
| n   | 305                            | 122                             | 183                               |         |
| Race/ethnicity (%)  |                                |                                 |                                   | <0.0001 |
| White   | 73.0                           | 90.1                            | 61.8                              |         |
| African American  | 19.1                           | 6.6                             | 27.3                              |         |
| Other   | 7.9                            | 3.3                             | 10.9                              |         |
| Postmenopause   | 90.1                           | N/A                             | 90.1                              | n/a     |
| Age (years)   | 61.3 ± 6.5                     | 61.4 ± 7.1                      | 61.3 ± 6.1                        | 0.89    |
| BMI (kg/m <sup>2</sup> )                                      | 36.5 ± 5.8                     | 36.1 ± 5.6                      | 36.7 ± 5.9                        | 0.34    |
| Weight (kg)   | 101.7 ± 18.0                   | 110.9 ± 16.5                    | 95.6 ± 16.2                       | <0.0001 |
| Height (cm)   | 167.0 ± 9.7                    | 175.5 ± 7.0                     | 161.3 ± 6.6                       | <0.0001 |
| Waist circumference (cm)                                      | 115.0 ± 13.0                   | 120.9 ± 12.1                    | 111.0 ± 12.1                      | <0.0001 |
| Neck circumference (cm)                                       | 41.1 ± 4.4                     | 44.4 ± 3.2                      | 39.0 ± 3.1                        | <0.0001 |
| A1C   | 7.2 ± 1.1                      | 7.4 ± 1.1                       | 7.1 ± 1.0                         | 0.03    |
| Total sleep time (h)  | 6.0 ± 1.2                      | 5.8 ± 1.3                       | 6.1 ± 1.1                         | 0.03    |
| Sleep efficiency (%)  | 77.5 ± 11.1                    | 77.1 ± 11.8                     | 77.7 ± 10.6                       | 0.69    |
| Time in non-REM stages (h)                                    | 4.9 ± 1.0                      | 4.9 ± 1.1                       | 5.0 ± 1.0                         | 0.32    |
| Time in REM stages (h)  | 1.0 ± 0.5                      | 0.9 ± 0.5                       | 1.1 ± 0.5                         | 0.002   |
| Sleep time supine (h)   | 2.1 ± 2.0                      | 1.9 ± 1.9                       | 2.2 ± 2.1                         | 0.21    |
| Obstructive apnea index                                       | 11.1 ± 12.8                    | 14.2 ± 15.5                     | 9.1 ± 10.2                        | 0.008   |
| Central apnea index   | 0.4 ± 1.0                      | 0.6 ± 1.2                       | 0.3 ± 0.7                         | 0.003   |
| Hypopneas with ≥4% oxygen desaturation*                       |                                |                                 |                                   |         |
| Apnea-hypopnea index  | 20.5 ± 16.8                    | 24.6 ± 18.6                     | 17.8 ± 15.0                       | 0.001   |
| Hypopnea index  | 9.0 ± 8.1                      | 9.8 ± 8.3                       | 8.4 ± 8.0                         | 0.16    |
| Oxygen desaturation index (≥4%)†                              | 17.6 ± 14.7                    | 20.0 ± 15.9                     | 15.9 ± 13.7                       | 0.03    |
| Participants that spent >10% of time below 90% saturation (%) | 16.1                           | 20.5                            | 13.1                              | 0.11    |
| Oxygen saturation nadir                                       | 81.4 ± 8.3                     | 81.2 ± 7.5                      | 81.6 ± 8.8                        | 0.65    |
| Epworth Sleepiness Score                                      | 7.9 ± 4.6                      | 8.0 ± 4.5                       | 7.8 ± 4.7                         | 0.80    |

Data are means ± SD. \*See Ref. 5. †Based on oxygen desaturation events ≥4% (5). REM, rapid eye movement.

(3.1 ± 1.0 Sleep AHEAD; 2.8 ± 1.1 Look AHEAD,  $P < 0.01$ ) (1 = do not snore anymore, to 4 = 6–7 nights per week) and in those already diagnosed with OSA (7.6% Sleep AHEAD; 13.4% Look AHEAD,  $P < 0.01$ ). There were no differences in the presence or loudness of snoring or excessive daytime sleepiness. No symptoms assessed in this study predicted the presence or severity of OSA.

### Sleep-disordered breathing

Only 13.4% of participants did not have OSA, whereas 33.4% had mild OSA, 30.5% moderate OSA, and 22.6% severe OSA. Similar findings were obtained in participants who did not have a previous diagnosis of OSA and had not been prescreened based on symptoms ( $n = 202$ ). Males had a higher AHI than females. BMI, sex, and waist and neck circumference were related to AHI. Waist circumference was the only significant predictor (odds ratio [OR] 1.1; 95% CI 1.0–1.1;  $P = 0.03$ ) of the presence of OSA (AHI ≥5). Independent of other variables, a

1-cm increase in waist circumference was associated with a 10% increase in the predicted odds of the presence of OSA (AHI ≥5).

In participants with AHI ≥5 ( $n = 264$ ), BMI was the only significant predictor of severe OSA (OR 1.1; 95% CI 1.0–1.2;  $P = 0.03$ ). Independent of other variables, a 1-unit increase in BMI was associated with a 10% increase in the predicted odds of severe OSA. Sex approached significance. Males were 2.2 times more likely to have severe OSA than females (OR 2.2; 95% CI 0.9–5.3;  $P = 0.08$ ). In the full sample ( $n = 305$ ), waist circumference was the only statistically significant predictor of continuous AHI ( $\beta = 0.02$ , 95% CI 0.01–0.03;  $P = 0.04$ ). None of the interaction terms was statistically significant.

**CONCLUSIONS**— The most remarkable finding of this study is the exceedingly high prevalence of undiagnosed OSA (86.6%) among obese patients with type 2 diabetes. These data

were suggested by earlier studies of smaller samples and/or that used less than full polysomnography to assess AHI (8–10). Equally alarming is the unequivocally elevated mean AHI (20.5 ± 16.8) of this group and that 22.6% of participants had severe OSA. Even though obesity, age, and menopause are known risk factors for OSA (11–13), the extraordinarily high rates of undiagnosed and severe OSA in this cohort are remarkable. Given the similarities between the participants in Sleep AHEAD versus Look AHEAD (but not in Sleep AHEAD), our results do not appear to be secondary to a selection bias. Potential links between OSA and type 2 diabetes have been recently reviewed (14). Definitive conclusions about the prevalence of OSA among individuals with type 2 diabetes require a control group without diabetes.

The second major finding was that waist circumference was the only significant predictor of the presence of OSA (AHI ≥5) (15). The failure of neck circumference and BMI to contribute to the

model is likely due to the restricted upper range of these variables in this sample compared with a community sample. Having a higher BMI, however, did increase the risk of severe OSA (AHI  $\geq$ 30).

**CONCLUSIONS**—Physicians treating obese patients with type 2 diabetes should consider the possibility of OSA, even in the absence of symptoms, especially in individuals with higher waist circumference and BMI. The high prevalence of OSA in obese patients with type 2 diabetes represents a serious public health problem and raises the possibility that some of the morbidity and mortality associated with type 2 diabetes may be attributable to undiagnosed OSA.

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