Weight Loss Is Integral to Obstructive Sleep Apnea Management

Ten-Year Follow-up in Sleep AHEAD

Excess weight is the strongest factor in the risk and severity of obstructive sleep apnea (OSA) (1). Two decades ago, prospective observational studies reported that a 10% weight gain over 4 years is associated with a 32% increase in the apnea–hypopnea index (AHI) and, conversely, a 10% weight loss predicts a 26% decrease in AHI (2). More recently, randomized controlled trials (RCTs) with up to 4-year follow-up indicated that weight loss is associated with decreased OSA severity with an average change in AHI of 0.78 events/h for every kilogram of weight lost, and that a small proportion of patients can achieve remission of OSA (AHI $<$ 5 events/h) (3, 4).

In this issue of the *Journal*, Kuna and colleagues (pp. 221–229) report on change in AHI at 10-year follow-up in Sleep AHEAD (Action for Health in Diabetes), a multicenter RCT of 306 middle-aged and older adults with overweight or obesity and type 2 diabetes (5). Participants who had OSA at baseline ($n = 264$; AHI $\geq$ 5 events/h, mean age 61.3 yr, and mean body mass index 36.6 kg/m^2) were randomized to receive either intensive lifestyle intervention (ILI) aimed at reducing body weight by at least 10% within 1 year or diabetes support and education (DSE) as part of standard care (control group). This is the longest RCT to date reporting on OSA trajectories in adults undergoing a lifestyle weight management program. Added strengths include the rigorous RCT design, AHI assessment by polysomnography at baseline and Years 1, 2, 4, and 10, and the use of high standards to minimize interscorer variability.

There are several noteworthy findings in this report by Kuna and colleagues. The authors found that the greater reductions in body weight and AHI in the ILI group compared with DSE, which were evident at 1-, 2-, and 4-year follow-ups (6), persisted at 10-year follow-up, albeit with some attenuation over time (Table 1). Of note, despite a significantly greater weight loss by 3.6 kg with ILI over DSE at 10 years, the reduction in AHI favoring ILI by 4.0 events/h did not reach statistical significance between intervention arms. Nevertheless, considering all follow-up visits, the overall intervention effect resulted in a 7.4 events/h greater reduction in AHI with ILI. At 10-year follow-up, for every kilogram of weight lost in ILI participants relative to baseline, the AHI decreased by 0.68 events/h compared with 0.54 events/h in DSE participants (*P* value not reported). From Year 4 to Year 10, both groups showed reductions in weight and AHI, and curiously, for every kilogram of weight lost during this period, the AHI decreased by 3.1 events/h in ILI compared with 3.8 events/h in DSE. This suggests that unmeasured factors between 4-year and 10-year follow-ups may have contributed to the observed modestly greater intervention effects on AHI in the control group. At 10 years, the remission of OSA was more common in ILI (34.4%) than in DSE (22.2%) participants, particularly in those who had mild to moderate OSA. Taken together, the findings by Kuna and colleagues highlight the importance of weight management in OSA, particularly in patients with type 2 diabetes, regardless of type of intervention used to achieve weight loss. Indeed, weight loss by either medical or surgical approaches has beneficial effects on OSA severity and glycemic control, and it can potentially cure OSA in some patients (4).

Interestingly, the authors found that although the change in weight predicted the improvement in AHI over time, weight loss alone did not explain the full extent of the intervention effects on OSA severity. Additionally, changes in waist circumference, a surrogate marker of visceral adiposity, did not independently influence AHI. So, what could be the potential explanations for these intriguing weight-independent intervention effects? In Sleep AHEAD, lifestyle intervention focused on modifications of diet and physical activity, and perhaps these healthier lifestyle behaviors contributed to the reduction in AHI. In adults from diverse backgrounds, diet quality is associated with OSA severity, after adjusting for confounders (7). To our knowledge, diet data are not available from Sleep AHEAD. Also, independent of body habitus, level of exercise is associated with OSA severity (8). Although physical activity data were not included in this report by Kuna and colleagues, the authors previously found that cardiorespiratory fitness does not predict change in AHI at 4-year follow-up, after adjusting for change in weight (9). There is evidence from RCTs to suggest that diet-only, exercise-only, and combined diet and exercise interventions all attenuate OSA severity despite highly variable changes in weight (10). These weight-independent effects of intervention on OSA severity are likely due to multifactorial mechanisms that may modulate upper airway stability, chemoreceptor sensitivity, visceral adiposity, neuroendocrine control, sleep quality, and other aspects of OSA pathophysiology, which are yet to be discovered (10–12).

It is worth noting that these new insights from Sleep AHEAD by Kuna and colleagues should be interpreted cautiously given some limitations. First, the sleep studies were missing in about half of the participants at the 10-year follow-up. The authors performed *post hoc* statistical analyses (e.g., multiple imputations and weighing for missingness) in an attempt to address this drawback. Sensitivity analyses in 96 participants who had complete AHI data at 10 years would have been useful to further support the authors' conclusions. Second, 16% of patients were receiving continuous positive airway pressure treatment for OSA, which may partly bias measured outcomes. Third, the potential effects of changes in medications that commonly influence weight (13), in particular the use of oral antidiabetic agents or insulin in this diabetic population, could be confounders. Lastly, Sleep AHEAD involved older adults with overweight/obesity and type 2 diabetes, which may limit the generalizability to more diverse populations.

Weight loss is frequently recommended to patients with OSA with overweight and obesity (4). Although Kuna and colleagues found no statistically significant difference in OSA severity at

E.T. is funded by NIH R01 DK120312-01A1 and R01DK115471. M.-P.S.-O. is funded by NIH R01HL128226 and R01HL142648 and AHA 16SFRN27950012.

Originally Published in Press as DOI: 10.1164/rccm.202007-2906ED on August 14, 2020

Table 1. ILI versus DSE

	1-yr Follow-up		2-yr Follow-up		4-yr Follow-up		10-yr Follow-up	
	ILI Group	DSE Group	ILI Group	DSE Group	ILI Group	DSE Group	ILI Group	DSE Group
Polysomnography, *n* (%)*	103 (82)	116 (83)	99 (79)	111 (80)	82 (66)	83 (60)	67 (54)	67 (48)
Change in weight, kg†	−10.7	−0.5	−7.4	−0.8	−5.1	−0.9	−7.1	−3.5
Change in AHI, events/h†	−5.5	4.3	−3.6	4.4	−3.8	4.0	−9.9	−5.9
Change in waist circumference, cm†	−9.0	−0.6	−5.9	−0.7	−3.4	0.2	−2.1	1.6
Remission of OSA, %‡	13.6	3.5	Data not published	Data not published	20.7	3.6	34.4	22.2

Definition of abbreviations: AHI = apnea–hypopnea index; DSE = diabetes support and education; ILI = intensive lifestyle intervention; OSA = obstructive sleep apnea.
Data are means unless otherwise specified.
*The number (% of total) of participants who had available polysomnography data among *n* = 264 total participants who were randomized.
†Change from baseline; all comparisons are statistically significant between the ILI and DSE groups except for change in AHI at 10-year follow-up.
‡One-year follow-up data are from Reference 15; 2-year follow-up data have not been published.

10-year follow-up between active and control intervention arms, their overall conclusions clearly support the potential benefit of weight loss on OSA severity in the long term with the possibility of remission of OSA in some patients. These findings also provide an important message that lifestyle modifications combining healthy diet and exercise should be integral to OSA management, particularly in patients with type 2 diabetes. Further research efforts should focus on testing whether lifestyle interventions for weight loss combined with continuous positive airway pressure treatment of OSA lead to synergistic effects in mitigating cardiometabolic consequences of OSA (14). ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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