



Weighing the Impact of CPAP Therapy on Body Mass in Persons With OSA

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Citation	Budhiraja, Rohit, Stuart F. Quan. "Weighing the Impact of CPAP Therapy on Body Mass in Persons With OSA" CHEST 155, issue 4 (2019): 657 - 658
Citable link	http://nrs.harvard.edu/urn-3:HUL.InstRepos:42656567
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Word Count: 999

To accompany manuscript # CHEST-18-1406.R1

Editorial

Weighing the impact of CPAP therapy on body mass in persons with OSA

**Rohit Budhiraja, M.B.B.S.
rbudhiraja@bwh.harvard.edu**

**Stuart F. Quan, M.D.
Stuart_Quan@hms.harvard.edu**

Title of first author: Assistant Professor of Medicine, Harvard Medical School and Medical Director, Sleep Disorders Clinic, Brigham and Women's Faulkner Hospital

Complete contact address:

1153 Centre Street

Suite 5K

Boston, MA 02130

Voice: 617-983-7489

Fax: 617-983-2488

Email: rbudhiraja@bwh.harvard.edu

**Correspondence to: Stuart F. Quan, M.D.
Stuart_Quan@hms.harvard.edu**

Conflict of interest statements for all authors -

Dr. Quan serves as a consultant for Jazz Pharmaceuticals and Best Doctors, and receives grant funding from the National Institutes of Health. Dr.

Budhiraja has indicated no conflicts of interest.

Weighing the impact of CPAP therapy on body mass in persons with OSA

Several studies have demonstrated that when used adequately, continuous positive airway pressure (CPAP) therapy mitigates several negative consequences of obstructive sleep apnea (OSA) including excessive sleepiness and hypertension, and improves quality of life.^{1,2} However, concerning is the observation by several researchers that use of CPAP has been associated with weight gain.^{3,4} This is a bothersome finding because increased weight is generally associated with the development or worsening of OSA and adverse health outcomes. Furthermore, a fear of weight gain might negatively influence OSA patients' decision to accept or be adherent to CPAP therapy.

Several mechanisms have been hypothesized whereby CPAP therapy may modulate body mass in persons with OSA. Diminished sleep quality and daytime fatigue, hallmarks of OSA, may limit physical activities. Furthermore, sleep disruption has been associated with increased caloric intake.⁵ OSA has also been suggested to alter leptin secretion or sensitivity.⁶ Finally, chronic sleep fragmentation and hypoxemia from OSA may alter the gastric microbiota, which may predispose to weight gain.⁷ Traditionally, it has been assumed that CPAP therapy of OSA would reverse these pathophysiologic alterations and result in weight loss. Thus, the etiology of unexpected gain in weight in previous studies is not entirely clear. Modifications in leptin levels, inflammatory cytokines, growth hormone axis and decreased energy expenditure have been suggested as possible mechanisms for the reported weight gain.⁸ CPAP may reduce the resting metabolic rate without an appreciable impact on physical activity levels.⁹ One study found that increase in weight after CPAP therapy correlated with insulin resistance.¹⁰ However, some recent studies involving a more detailed analysis of weight gain have suggested that the weight gain may actually result from an increase in lean mass rather than body fat.¹¹

In view of the limitations of the current literature regarding weight modulation with CPAP, additional studies evaluating this relationship might be further informative. To this end, Ou et al present post hoc analysis of weight and other anthropometric data from the SAVE trial, a randomized secondary prevention trial of CPAP vs. sham CPAP to treat OSA in persons with a prior diagnosis of cardiovascular or cerebrovascular disease.¹² The authors analyzed data from 2,483 adults with co-morbid OSA and cardiovascular disease, who were followed for a mean of 3.8 years. Except for an increase in weight among males using CPAP in their propensity matched subgroup analysis, no increase in weight or BMI was noticed in either the CPAP or sham CPAP group.

The paper is well-written and the proposed conclusions clear. The study itself has several strengths. It was a multicenter, randomized trial. The number of participants was substantial, 1,248 in the CPAP group and 1,235 in the control group, and the mean follow up was almost 4 years. The study cohort had representation from different countries, and hence, diverse populations. However, this may have been a major limitation as well. Approximately 2/3rds of the participants were recruited from China. It is well established that Asians with OSA are less obese than their Caucasian counterparts in Western countries. Several studies have suggested that being overweight, while still an important factor in causation of OSA,

may not be the decisive predictor of this disorder in the Chinese population. A more crowded posterior oropharynx may be a conspicuous contributor to OSA in Chinese.¹³ Persons from India also have more severe sleep apnea for the same level of obesity when compared to Caucasians,¹⁴ suggesting that factors other than obesity may contribute significantly to the pathogenesis of OSA in this population as well. Indeed, these two groups of participants demonstrated weight loss with OSA therapy in this study. In contrast, weight gain was observed in participants recruited from New Zealand.

While it is reassuring that no weight gain was noticed in this study, it is difficult to extrapolate this finding to Western countries. In a meta-analysis by Drager et al, the mean BMI was $\sim 31.3 \text{ kg/m}^2$. The largest component study included was the cohort from APPLES, a study from North America in which the mean BMI of the participants was 32.3 kg/m^2 . The mean BMI of participants in the current study was $<30 \text{ kg/m}^2$. It is conceivable that the results of the study would have been different if the predominant race of the participants had been Caucasian and had a higher BMI.

Another concern is the low adherence in both the CPAP and sham CPAP groups. If the adherence to CPAP had been greater, mechanisms favoring weight gain in the CPAP group might have had a greater influence. Evidence supporting this possibility can be found in the Ou et al's propensity subgroup analysis where men with adherence $> 4\text{h}$ demonstrated weight gain.

Despite these concerns, the current study is an important addition to the literature regarding CPAP therapy and weight change. Future studies should aim to address some of the following questions. Are there changes in weight amongst different age groups, genders, ethnicities and race? Are there any polysomnographic/ sleep predictors of weight change? If weight gain occurs with CPAP, is it comprised primarily of lean mass gain or increased body fat percent? With the advent and rise of 'Big Data' in the field of Sleep Medicine, the answers to these questions may be more readily forthcoming.¹⁵ Use of electronic health records can facilitate tracking and analyzing of several variables over long intervals. Smartphones and wearables are becoming ubiquitous and tracked data frequently includes weight, physical activity, sleep and nutrition. Patient generated health data may thus further help unconfound these issues.

Although Ou et al did not find that CPAP use resulted in weight gain, the most important message for clinicians from this study is that significant weight loss did not occur. Therefore, clinicians should reiterate the benefits of weight loss to their OSA patients as well as provide them with options to effectuate weight loss at every possible opportunity. A comprehensive approach to weight loss should be used instead of the optimistic view that improved sleep quality and daytime symptoms will automatically translate into increase physical activity, better nutrition and weight loss.

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