



Contribution of central sleep apnea to severe sleep apnea hypopnea syndrome

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Abstract

Purpose Central sleep apnea (CSA) is usually distinguished from obstructive sleep apnea (OSA). In fact, CSA is often a component of severe sleep apnea hypopnea syndrome (SAHS), rather than occurring alone. We investigated the clinical characteristics and polysomnography (PSG) parameters of CSA components in patients with severe SAHS.

Methods The clinical characteristics and PSG parameters were retrospectively analyzed.

Results Pure or dominant CSA was rare (5% of all patients). Of all patients with CSA, 72% also exhibited other apnea subtypes that contributed to severe SAHS. Among patients with severe SAHS, those with CSA were more likely than others to be older; thinner; exhibit higher prevalences of comorbid coronary heart disease, arrhythmia, and heart failure; a higher apnea/hypopnea index (AHI); mixed apnea index (MAI); an elevated oxygen desaturation index (ODI); and more nighttime oxygen saturation levels < 90%. Multivariate logistic regression analysis revealed that older age, comorbid arrhythmia or heart failure, and an elevated ODI were independently associated with CSA.

Conclusion Patients who complain of snoring or apnea may be better evaluated by comprehensive PSG prior to treatment if they are old, show greater hypoxia, or suffer from arrhythmia and/or heart failure, because such patients are more likely than others to exhibit CSA.

Keywords Central sleep apnea (CSA) · Mixed sleep apnea (MSA) · Arrhythmia · Heart failure

Introduction

Obstructive sleep apnea (OSA) is very common and is characterized by recurrent episodes of upper airway collapse leading to complete or partial cessation of airflow even with respiratory effort [1]. By contrast, central sleep apnea (CSA), characterized by respiratory apnea accompanied by a lack of respiratory effort during sleep, is much less common, except in patients with cardiac diseases or those who take opiates [2–4]. Previous studies have focused on patients with

dominant CSA, regardless of the severity of sleep apnea hypopnea syndrome (SAHS) [5–7]. However, it is noteworthy that CSA is typically comorbid with OSA, mixed sleep apnea (MSA), and hypopnea. These types of SAHS may constitute a severe phenotype (the apnea/hypopnea index [AHI] is ≥ 30) together, which may be more harmful and deserving treatment. Continuous positive airway pressure ventilation (CPAP) may be used to treat suspected OSA directly. But for those patients with a component of CSA, there may be a greater possibility of complex sleep apnea syndrome or lower adherence to CPAP therapy [8–10]. The home sleep apnea test (HSAT) detects OSA in a cost-effective manner but does not distinguish CSA [8, 11]. To allocate medical resources optimally and to ensure appropriate treatment, it is important to be alert for CSA in patients with SAHS irrespective of which apnea subtype predominates. We therefore explored the clinical characteristics and PSG parameters of patients with severe SAHS with and without CSA regardless of whether or not CSA predominated. We also sought indicators of CSA events in an effort to facilitate appropriate diagnosis and treatment.

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Methods

Subjects

Patients who complained of snoring or apnea and who underwent overnight PSG in the Sleep Center of Tianjin Chest Hospital were retrospectively enrolled from January 2015 to March 2022. The exclusion criteria were total sleep time < 120 min, long-term sedative or sleeping tablet usage, any prior SAHS diagnosis, and noninvasive positive pressure ventilation treatment. We defined pure CSA as a central apnea index (CAI) ≥ 5 with a respiratory event index of any/all other subtype(s) < 5; dominant CSA as an AHI ≥ 5 and a CAI-to-AHI ratio > 50%; and secondary CSA as an AHI ≥ 5 and a CAI ≥ 5 and a CAI-to-AHI ratio $\leq 50\%$. When exploring the contributions of CAI to severe SAHS, we divided patients into a wCSA group (AHI ≥ 30 and CAI ≥ 5) and an nCSA group (AHI ≥ 30 and CAI < 5). We recorded sex, age, height, weight, neck and waist circumference, and comorbidities. The body mass index (BMI) was the weight in kilograms divided by the square of the height in meters. Atrial arrhythmia was defined as persistent atrial fibrillation (AF) or atrial flutter. Heart failure was defined by a previous diagnosis via echocardiography, assay of the brain natriuretic peptide (BNP) level, or obvious symptoms.

PSG

Overnight PSG yielded electroencephalography data (F_4/M_1 , C_4/M_1 , O_2/M_1 , F_3/M_2 , C_3/M_2 , O_1/M_2) and also included electrooculography, submental electromyography, bilateral anterior tibialis electromyography, and electrocardiography. Respiratory inductance plethysmography was used to monitor the respiratory effort of thoracoabdominal movement. Airflow was assessed using oronasal thermal and pressure sensors. A finger pulse oximeter was employed to record oxygen saturation. Sleep stages were manually assessed using the 2012 American Academy Sleep Medicine criteria [4]. Apnea was defined as an airflow reduction > 90% of the pre-event baseline for ≥ 10 s; hypopnea was defined as a reduction in airflow $\geq 30\%$ of the pre-event baseline for ≥ 10 s with $\geq 3\%$ oxygen desaturation. OSA and CSA events were defined as apneas in the presence or absence of respiratory effort, respectively. Mild, moderate, and severe SAHS were defined as $5 \leq \text{AHI} < 15$ events/h, $15 \leq \text{AHI} < 30$ events/h, and $\text{AHI} \geq 30$ events/h, respectively. The oxygen desaturation index (ODI) was the number of times in which oxygen saturation decreased by 3%/h.

Statistical analysis

Normally distributed quantitative data are presented as means \pm standard deviations and non-normally distributed

data are given as medians with interquartile ranges. Qualitative data are expressed as frequencies with percentages. Numerical variables were compared using the independent paired *t*-test and the Mann-Whitney *U*-test for normally and non-normally distributed data, respectively. Categorical variables were compared employing the chi-square or Fisher exact test (as appropriate). Only variables with *P*-values < 0.1 were included in multivariate logistic regression, except cerebrovascular disease. In view of the difference in the prevalence of cerebrovascular disease between the two groups and the important influence of cerebrovascular disease on CSA, cerebrovascular disease (*P* = 0.324) was also included in the multivariate regression analysis. For all analyses, a two-tailed *P* < 0.05 was considered significant. All analyses were performed using SPSS ver. 25 software.

Results

Subtypes of patients who underwent PSG

Of 714 patients who met the inclusion criteria, 123 (17%) had CSA and 3 (2%), 13 (11%), and 107 (87%) for mild, moderate, and severe SAHS, respectively. In all, 10 patients (8%) had pure CSA, 24 (20%) had dominant CSA, and 89 (72%) had secondary CSA (Figure 1A). Thus, most CSA events were comorbid with other apnea subtypes; such combinations constituted severe SAHS. In 553 patients with severe SAHS, 107 (19%) exhibited CSA (CAI ≥ 5 , defined as wCSA group) but 446 (80%) did not (CAI < 5, defined as nCSA group). In the wCSA group with severe SAHS, dominant CSA accounted for only 20% of patients (21/107). Among patients with severe SAHS, both with and without CSA, obstructive apneas were the most common type of events (Figure 1B).

Characteristics, comorbidities, and PSG parameters

We included 553 patients with severe SAHS. Most were males (466, 84%) of mean age 52.7 ± 12.1 years with a median AHI of 51.6 (39.2, 64.4)/h. Patients with (compared to without) CSA were older, thinner, and more likely to exhibit comorbid coronary heart disease, arrhythmia, and heart failure (all *P* < 0.05). Sex and neck and waist circumference did not differ between the two groups; neither did the prevalence of diabetes, cerebrovascular or chronic airway inflammatory disease, or pulmonary embolism (Table 1). Compared to the nCSA group, wCSA patients had a higher AHI and MAI but a lower OAI and hypopnea index (HI). The REM and NREM percentages of total sleep time (TST) did not significantly differ. The percent of night oxygen saturation < 90% (Tsat90) was somewhat greater in the wCSA group, but the ODI was significantly higher (Table 2).

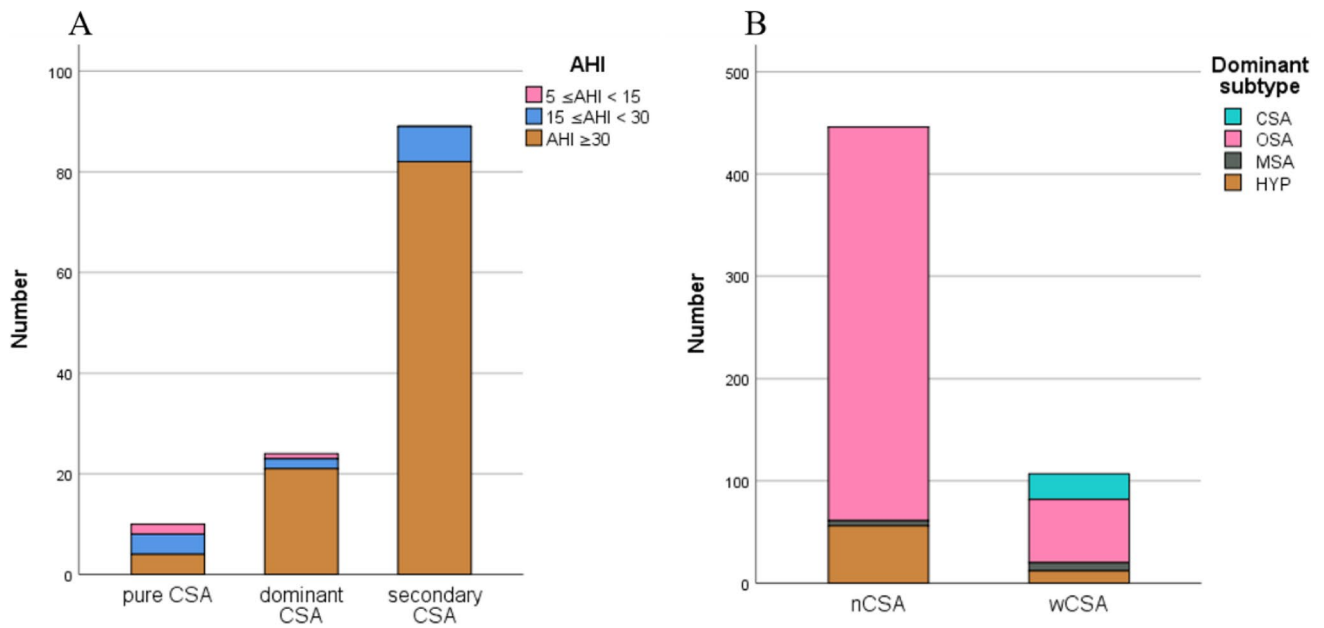


Fig. 1 Apnea subtypes of SAHS patients, and SAHS severities. **A** Secondary CSA patients were much more common than pure and dominant CSA patients. The severe SAHS phenotype predominated in both the dominant and secondary CSA groups. **B** 553 patients with severe SAHS (AHI≥30, dominant subtype unspecified) were

divided into wCSA group and nCSA group according to CSA existed (CAI≥5) or not. Patients lacking CSA (nCSA) were much more common than those with CSA (wCSA). The OSA subtype predominated in both groups, followed by hypopnea (HYP), and then MSA, grouping variable CSA not included

Table 1 Characteristics and comorbidities of the nCSA and wCSA groups

Parameter	wCSA (n = 107)	nCSA (n = 446)	P-value
Demographic characteristics			
Males, N (%)	91 (85)	375 (84)	0.805
Age, M ± SD (years)	56.2 ± 11.5	51.8 ± 12.1	0.001**
Anatomical characteristics, m (P25, P75)			
BMI	28.8 (26.2, 31.5)	29.7 (27.2, 32.9)	0.036*
Neck circumference	42.0 (40.0, 45.0)	43.0 (40.0, 45.0)	0.465
Waist circumference	105.0 (98.0, 112.0)	106.0 (99.0, 114.0)	0.500
Comorbidities, N (%)			
Hypertension	55 (51)	185 (42)	0.063
Coronary heart disease	34 (32)	95 (21)	0.021*
Arrhythmia	22 (21)	35 (8)	<0.001***
Heart failure	5 (5)	2 (0)	<0.001***
Diabetes	14 (13)	57 (13)	0.933
Cerebrovascular disease	1 (1)	14 (3)	0.324
Chronic airway inflammatory disease	2 (2)	22 (5)	0.196
Pulmonary embolism	3 (3)	7 (2)	0.416

M ± SD = mean ± standard deviation, m = median, P25 = 25th percentile, P75 = 75th percentile. *P < 0.05, **P < 0.01, ***P < 0.001 vs. the nCSA group

Correlations between the CSA and other parameters

Only variables with P-values < 0.1 in univariate analysis were included in multivariate logistic regression analysis, with the exceptions of the MAI and HI (only the AHI was

included because the AHI is strongly associated with the MAI, CAI, and HI), and exceptions of cerebrovascular disease due to the reasons mentioned above. Older age, a greater ODI, arrhythmia, and heart failure independently predicted comorbid CSA in patients with severe SAHS

Table 2 PSG parameters of the nCSA and wCSA groups

PSG parameter	wCSA (n = 107)	nCSA (n = 446)	P-value
AHI	55.1 (42.5, 65.3)	50.7 (38.2, 64.2)	0.039*
CAI	10.2 (6.9, 21.1)	0.2 (0, 1.4)	<0.001***
REM-CAI	11.1 (3.1, 28.3)	0 (0, 1.1)	<0.001***
NREM-CAI	10.4 (6.6, 20.7)	0.2 (0, 1.3)	<0.001***
OAI	22.5 (10.4, 38.1)	37.6 (24.6, 53.0)	<0.001***
REM-OAI	14.4 (6.5, 29.7)	37.0 (22.2, 51.6)	<0.001***
NREM-OAI	18.9 (8.8, 34.4)	38.2 (22.8, 50.2)	<0.001***
MAI	5.5 (2.0, 14.4)	0.7 (0.1, 2.7)	<0.001***
REM-MAI	2.2 (0.0, 11.7)	0.0 (0.0, 2.7)	<0.001***
NREM-MAI	3.8 (1.3, 13.9)	0.3 (0.0, 2.9)	<0.001***
HI	4.9 (2.1, 10.8)	7.3 (3.2, 14.1)	0.015*
REM-HI	3.5 (0.5, 11.8)	6.0 (1.1, 14.5)	0.133
NREM-HI	5.9 (2.2, 12.9)	7.4 (3.0, 15.5)	0.183
Percent REM	18.2 (6.3, 26.1)	14.2 (4.8, 22.6)	0.052
Percent NREM	81.8 (73.9, 93.7)	85.7 (77.4, 95.2)	0.050
Mean SpO ₂ (%)	92.6 (90.8, 94.0)	93.0 (91.6, 95.0)	0.120
REM-Mean SpO ₂ (%)	92.0 (89.9, 93.9)	92.9 (90.6, 94.5)	0.025*
NREM-Mean SpO ₂ (%)	92.5 (91.0,94.0)	93.2 (91.6, 95.0)	0.094
Lowest SpO ₂ (%)	75.0 (66.0, 81.0)	76.0 (66.0, 81.0)	0.945
Tsat90 (%)	16.7 (3.9, 31.4)	9.5 (3.0, 26.4)	0.043*
Tsat80 (%)	0.2 (0, 2.9)	0.2 (0, 2.5)	0.994
ODI	43.0 (31.7,57.8)	37.0 (23.3, 54.4)	0.007**

Data are shown as medians (P25, P75). *AHI*, apnea/hypopnea index; *CAI*, central apnea index; *OAI*, obstructive apnea index; *MAI*, mixed apnea index; *HI*, hypopnea index; *REM*, rapid eye movement; *NREM*, non-rapid eye movement; *SpO₂*, pulse oxygen saturation; *Tsat90*, percentage of cumulative night time at an oxygen saturation less than 90%; *ODI*, oxygen desaturation index. **P* < 0.05, ***P* < 0.01, ****P* < 0.001 vs. the nCSA group

(Table 3). The area under the receiver operator curves for these four variables (combined) was 0.690 (95% confidence interval 0.634–0.747, *P* < 0.001). The predictive sensitivity was 62.3% and the specificity was 68.3% (Figure 2).

Discussion

We found that true CSA (defined as pure and dominant CSA in this article) was rare; the prevalence was 5% (34/714) in our general cohort. The majority of patients with CAIs ≥ 5 exhibited complex phenotypes with CSA components; they had severe SAHS. Patients with CSA differed from others in terms of age, BMI, comorbidities (coronary heart disease, arrhythmia, heart failure), the respiratory event indices, and the extent of oxygen desaturation.

A retrospective study in military veterans indicated that the prevalence of CSA was 0.6%, of which 64.1% was comorbid with OSA [5]. Lucas et al. reported a CSA prevalence of 0.9% in a community population [7], but 1.8% for males and 2.7% for males aged ≥ 65 years. Bixler et al. studied community males; the CSA prevalence was low (0.4%) but increased monotonically with age [12]. A clinical study reported a

Table 3 Association of CSA events with clinical and PSG parameters: results of multivariate logistic regression analysis

Variables	OR	95% C.I.	P	
Age	1.04	1.01	1.06	0.001**
BMI	1.01	0.99	1.02	0.606
Hypertension	1.17	0.71	1.91	0.537
Coronary heart disease	1.02	0.57	1.82	0.952
Arrhythmia	2.16	1.08	4.33	0.030*
Heart failure	12.19	1.88	79.08	0.009*
cerebrovascular disease	0.17	0.02	1.51	0.110
ODI	1.02	1.00	1.04	0.022*
AHI	1.01	0.99	1.03	0.606
Percent-REM	2.07	0.39	10.98	0.395
Tsat90	0.99	0.97	1.00	0.085

C.I., confidence interval. **P* < 0.05, ***P* < 0.01 vs. the nCSA group

primary CSA prevalence of 3.8%, 64% of which was severe [6]. The prevalence has varied across studies. Clinical studies have reported higher prevalences than community-based works. Several studies have found that CSA patients are more likely to be male than those with OSA [5, 12, 13]. In our

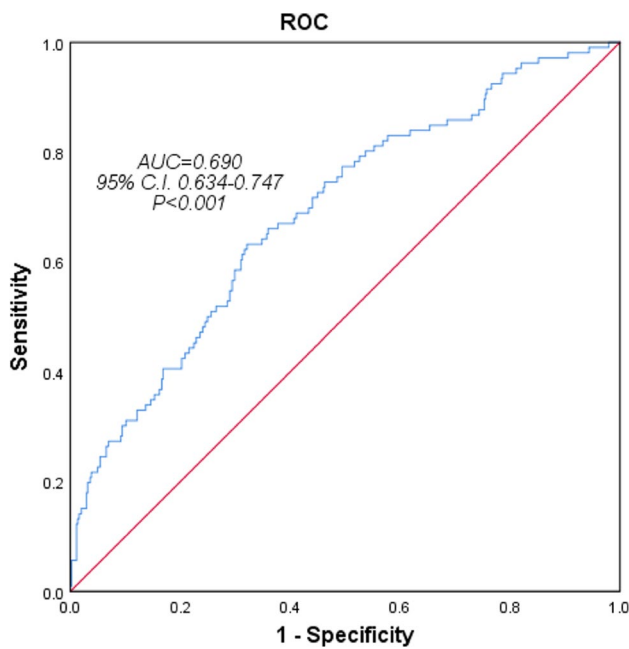


Fig. 2 ROC for the four variables combined

study, males were much more common than females in both groups, but the proportions were similar in the two groups (85.0 vs. 84.1%, $P = 0.805$), perhaps because wCSA features many OSA components. Several studies have found that CSA patients are thinner than controls [5, 7]. We similarly found that the BMI of the wCSA group was lower than that of the nCSA group (28.76 vs. 29.70 kg/m², $P = 0.026$).

OSA increases the risk for and progression of hypertension, type 2 diabetes, cardiovascular stroke, and atrial fibrillation [1, 14–17]. Strong associations between CSA and arrhythmias and heart failure have recently been reported. Harmon et al. found that the prevalence of OSA in AF and non-AF groups was similar (54.7 vs. 52.0%, $P = 0.56$) [18]. CSA was more common in their AF group (12.3 vs. 4.4%, $P = 0.002$). A prospective study showed that CSA (odds ratio [OR] 2.58, 95% CI 1.18–5.66) and CSA with Cheyne-Stokes breath (CSB) (OR 2.27, 95% CI 1.13–4.56), but not OSA, predicted incident atrial fibrillation [19]. The association was much stronger in patients aged ≥ 76 years. Another study drew similar conclusions: CSA and CSB were significantly associated with AF (OR 5.15, 95% CI 2.21–12.52 and OR 6.26, 95% CI 2.05–19.14, respectively) [20]. However, OSA was not significantly associated with AF. Grimm et al. found that the prevalence of CSA (AHI ≥ 15) was 43% in a cohort with left ventricular ejection fraction (LVEF) $\leq 50\%$. AF was strongly associated with severe CSA [21]. In a cohort of heart-failure patients with reduced or preserved LVEF, the LVEF correlated negatively with the CAI ($r = -0.558$, $P < 0.001$) but not with the OAI [22]. Thus, CSA is associated more strongly with AF and HF than OSA, despite the high prevalence of

OSA in AF and HF patients, perhaps because OSA per se is common in general populations. Our data are consistent with prior data. Compared to patients lacking CSA, the prevalences of arrhythmia (21 vs. 7.8%, $P < 0.001$) and heart failure (5 vs. 0.4%, $P < 0.001$) were higher in those with CSA.

In groups with and without CSA, OSA was the major component, and (unsurprisingly) the OAI was higher in the nCSA group. Notably, the MAI was significantly higher in the wCSA group, indicating a strong association with CSA. Mixed apnea features both central and obstructive components, and is usually considered an obstructive event [23]. Yamauchi et al. concluded that MSA is more closely associated with CSA than OSA, as revealed by instability of respiratory control; the cited authors studied respiratory signals and CPAP acceptance and compliance [24]. Yang et al. [25] found that MSA is linked to both a reduced mean oxygen saturation and the lowest oxygen saturation recorded, similar to what we found. Therefore, we hypothesize that both CSA and MSA are related to respiratory control unstable. We plan to investigate the potential for correlations between CSA and MSA events, and the loop gain and awakening threshold.

Regrettably, we did not categorize hypopnea into central or obstructive hypopnea using the 2012 Criteria of the American Academy of Sleep Medicine. In the clinic, we find it difficult to handle the inspiratory flattening/thoracoabdominal paradox. We may thus have underestimated central events. Central or obstructive events are optimally and precisely detected via esophageal, electrode catheter manometry [26], but patients dislike this.

As is true of all retrospective investigations, some patient data were lacking. In addition, selection bias may be in play; this would overestimate CSA events. However, this is the first work to view CSA events as components of severe SAHS; we did not focus on pure CSA. Patients with and without CA differed in terms of demography, complications, and PSG parameters. Physicians should have raised suspicion when patients are old, exhibit low oxygen saturation during sleep, and are comorbid with arrhythmia or heart failure.

In conclusion, CSA patients (compared to others) were older, more hypoxic, and more likely to suffer from arrhythmia and heart failure. Both MSA and CSA may be related to respiratory control instability. We recommend that patients with the above-mentioned risk factors undergo PSG rather than HSAT for the accurate diagnosis and appropriate therapy.

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Data availability The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare no competing interests.

Ethics approval and consent to participate All procedures performed in this study involving human subjects were in accordance with the ethical standards of the Ethics Committee of the Tianjin Chest Hospital and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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References

- Franklin KA, Lindberg E (2015) Obstructive sleep apnea is a common disorder in the population—a review on the epidemiology of sleep apnea. *J Thorac Dis* 7(8):1311–22. <https://doi.org/10.3978/j.issn.2072-1439.2015.06.11>
- Rana AM, Sankari A. (2022) Central sleep apnea. *StatPearls*, Treasure Island
- Eckert DJ, Jordan AS, Merchia P et al (2007) Central sleep apnea: pathophysiology and treatment. *Chest* 131(2):595–607. <https://doi.org/10.1378/chest.06.2287>
- Berry RB, Budhiraja R, Gottlieb DJ et al (2012) Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events Deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. *J Clin Sleep Med* 8(5):597–619. <https://doi.org/10.5664/jcsm.2172>
- Ratz D, Wiitala W, Badr MS et al (2018) Correlates and consequences of central sleep apnea in a national sample of US veterans. *Sleep* 08(41):9. <https://doi.org/10.1093/sleep/zsy058>
- Kouri I, Kolla BP, Morgenthaler TI et al (2020) Frequency and outcomes of primary central sleep apnea in a population-based study. *Sleep Med* 68:177–83. <https://doi.org/10.1016/j.sleep.2019.12.008>
- Donovan LM, Kapur VK (2016) Prevalence and characteristics of central compared to obstructive sleep apnea: analyses from the sleep heart health study cohort. *Sleep* 39(7):1353–9. <https://doi.org/10.5665/sleep.5962>
- Morgenthaler TI, Malhotra A, Berry RB et al (2021) Optimal NIV Medicare access promotion: patients with central sleep apnea: a technical expert panel report from the American College of Chest Physicians, the American Association for Respiratory Care, the American Academy of Sleep Medicine, and the American Thoracic Society. *Chest* 160(5):e419–e25. <https://doi.org/10.1016/j.chest.2021.07.039>
- Morgenthaler TI, Kagramanov V, Hanak V et al (2006) Complex sleep apnea syndrome: is it a unique clinical syndrome? *Sleep* 29(9):1203–9. <https://doi.org/10.1093/sleep/29.9.1203>
- Fashanu OS, Quan SF (2022) Factors associated with treatment outcomes after use of auto-titrating CPAP therapy in adults with obstructive sleep apnea. *Sleep Breath*. <https://doi.org/10.1007/s11325-022-02590-6>
- Kapur VK, Auckley DH, Chowdhuri S et al (2017) Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med* 13(3):479–504. <https://doi.org/10.5664/jcsm.6506>
- Bixler EO, Vgontzas AN, Ten Have T et al (1998) Effects of age on sleep apnea in men: I Prevalence and severity. *Am J Respir Crit Care Med* 157(1):144–8. <https://doi.org/10.1164/ajrccm.157.1.9706079>
- Bixler EO, Vgontzas AN, Lin HM et al (2001) Prevalence of sleep-disordered breathing in women: effects of gender. *Am J Respir Crit Care Med* 163(3 Pt 1):608–13. <https://doi.org/10.1164/ajrccm.163.3.9911064>
- Mostafa SA, Mena SC, Antza C et al (2022) Sleep behaviours and associated habits and the progression of pre-diabetes to type 2 diabetes mellitus in adults: a systematic review and meta-analysis. *Diab Vasc Dis Res* 19(3):14791641221088824. <https://doi.org/10.1177/14791641221088824>
- May AM, Van Wagoner DR, Mehra R (2017) OSA and cardiac arrhythmogenesis: mechanistic insights. *Chest* 151(1):225–41. <https://doi.org/10.1016/j.chest.2016.09.014>
- Huang B, Liu H, Scherlag BJ et al (2021) Atrial fibrillation in obstructive sleep apnea: neural mechanisms and emerging therapies. *Trends Cardiovasc Med* 31(2):127–32. <https://doi.org/10.1016/j.tcm.2020.01.006>
- Linz B, Hohl M, Lang L et al (2021) Repeated exposure to transient obstructive sleep apnea-related conditions causes an atrial fibrillation substrate in a chronic rat model. *Heart Rhythm* 18(3):455–64. <https://doi.org/10.1016/j.hrthm.2020.10.011>
- Harmon EK, Stafford P, Ibrahim S et al (2020) Atrial fibrillation is associated with central sleep apnea in clinic patients undergoing diagnostic polysomnography. *J Arrhythm* 36(6):991–6. <https://doi.org/10.1002/joa3.12427>
- May AM, Blackwell T, Stone PH et al (2016) Central sleep-disordered breathing predicts incident atrial fibrillation in older men. *Am J Respir Crit Care Med* 193(7):783–91. <https://doi.org/10.1164/rccm.201508-1523OC>
- Anzai T, Grandinetti A, Katz AR et al (2020) Association between central sleep apnea and atrial fibrillation/flutter in Japanese-American men: the Kuakini Honolulu Heart Program (HHP) and Honolulu-Asia Aging Study (HAAS). *J Electrocardiol* 61:10–7. <https://doi.org/10.1016/j.jelectrocard.2020.05.005>
- Grimm W, Sass J, Sibai E et al (2015) Severe central sleep apnea is associated with atrial fibrillation in patients with left ventricular systolic dysfunction. *Pacing Clin Electrophysiol* 38(6):706–12. <https://doi.org/10.1111/pace.12495>
- Wang T, Yu FC, Wei Q et al (2022) Prevalence and clinical characteristics of sleep-disordered breathing in patients with heart failure of different left ventricular ejection fractions. *Sleep Breath*. <https://doi.org/10.1007/s11325-022-02611-4>

23. Sleep-related breathing disorders in adults: (1999) recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep* 22(5):667-89
24. Yamauchi M, Tamaki S, Yoshikawa M et al (2011) Differences in breathing patterning during wakefulness in patients with mixed apnea-dominant vs obstructive-dominant sleep apnea. *Chest* 140(1):54–61. <https://doi.org/10.1378/chest.10-1082>
25. Yang X, Xiao Y, Han B et al (2019) Implication of mixed sleep apnea events in adult patients with obstructive sleep apnea-hypopnea syndrome. *Sleep Breath* 23(2):559–65. <https://doi.org/10.1007/s11325-018-1745-0>
26. Luo YM, Tang J, Jolley C et al (2009) Distinguishing obstructive from central sleep apnea events: diaphragm electromyogram and esophageal pressure compared. *Chest* 135(5):1133–41. <https://doi.org/10.1378/chest.08-1695>

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