


# Clinical and PSG Characteristics Comparison of Central Sleep Apnea in the Elderly and Non-Elderly Patients

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**Objective:** To explore the characteristics of elderly patients with central sleep apnea (CSA).

**Methods:** This retrospective study divided 123 patients with CSA into elderly and non-elderly groups, and compared them in terms of demographic characteristics (age, BMI, etc), underlying diseases (hypertension, coronary heart disease, and cardiac arrhythmias, etc) and polysomnography parameters. Multiple linear regression analysis was conducted to investigate the potential risk factors of central apnea index (CAI).

**Results:** Compared with the non-elderly group, patients in the elderly group had lower body mass index, a higher proportion of comorbidities of coronary heart disease, arrhythmias, and diabetes, lower apnea-hypopnea index (AHI), obstructive apnea index (OAI) and oxygen desaturation index (ODI). CAI of the elderly group showed a trend higher than that of the non-elderly group with no statistical difference. However, the ratio of CAI to AHI in the elderly group was significantly higher (0.264 vs 0.154,  $P=0.003$ ). True CSA was less prevalent than companion CSA in both groups. The results of multiple regression analysis indicated CAI was independently associated with age ( $\beta=0.256$ ,  $P=0.005$ ), OAI ( $\beta=-0.543$ ,  $P<0.001$ ), MAI ( $\beta=-0.267$ ,  $P=0.005$ ), ODI ( $\beta=0.538$ ,  $P<0.001$ ), heart failure ( $\beta=0.300$ ,  $P<0.001$ ).

**Conclusion:** CSA typically coexists with other types of sleep apnea. Elderly CSA patients have characteristics such as a lower BMI, and a milder decrease in blood oxygen saturation, along with higher prevalence of arrhythmia and coronary heart disease. Age may be a potential risk factor for CSA.

**Keywords:** elderly people, sleep apnea, heart failure, oxygen desaturation index

## Introduction

Sleep apnea syndrome (SAS), characterized by recurrent episodes of apnea during sleep, is the second largest group of sleep disorders. Cessation of oral and nasal airflow but presence of chest and abdominal movements are the hallmarks of obstructive sleep apnea (OSA), the most common and well-studied type of sleep apnea. However, central sleep apnea (CSA), which results in the cessation of both oronasal airflow and thoracoabdominal movements, is much less common and not well understood.<sup>1-4</sup>

CSA is not frequently diagnosed in the general population. Some specific types of CSA are secondary to CPAP treatment, high altitude residence, or intake of opioids, but otherwise, CSA is usually not easy to identify. Snoring, a prominent symptom in OSA, is absent in CSA sometimes.<sup>5</sup> Daytime sleepiness and morning headaches caused by sleep fragmentation and intermittent hypoxia are common in both OSA and CSA.<sup>6</sup> Moreover, the related symptoms caused by CSA are often confused with the patients' underlying conditions and are difficult to distinguish.<sup>2,7</sup> CSA usually has a higher incidence in the population with heart failure, stroke, and neuromuscular disorders.<sup>8</sup> Evidence showed that incidence of CSA increases with age.<sup>3,9,10</sup> The risk factors for the increased incidence of CSA in the elderly include weakened sleep stability, unstable respiratory regulation function, an increased proportion of cardiovascular disease, neurological disorders, and intakes of sedative hypnotic drugs.<sup>3,11,12</sup>

Unlike OSA, which is treated mainly with surgery and non-invasive positive pressure ventilation, CSA treatment includes drug intervention, oxygen therapy, adaptive servo-ventilation (ASV), and diaphragmatic pacing.<sup>13–15</sup> Therefore, it is crucial to identify the characteristics of CSA in the elderly to ensure correct diagnosis and appropriate treatment. However, there have been few studies on CSA in the elderly. Therefore, this study aimed to compare the characteristics of elderly and non-elderly patients with CSA and investigate the potential risk factors of CSA.

## Methods

### Subjects and Study Design

This retrospective study enrolled patients who were admitted to the Respiratory and Critical Care Medicine Department of Tianjin Chest Hospital, China, from January 2017 to March 2021 and had polysomnography (PSG) confirmed CSA. Patients' medical records were collected through an electronic case system and medical insurance system. We divided patients into elderly (aged  $\geq 65$  years) and non-elderly (aged  $< 65$  years) groups. We excluded patients with a total PSG monitoring time  $< 6$  hours, prolonged sedative and sleeping pill use, or previous diagnosis of sleep apnea or non-invasive positive pressure ventilation.

We recorded sex, age, height, weight, neck circumference, waist circumference, and comorbidities. The body mass index (BMI) is 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 Monitoring

Overnight PSG, which yielded electroencephalography data (F4/M1, C4/M1, O2/M1, F3/M2, C3/M2, and O1/M2), included electrooculography, submental electromyography, bilateral anterior tibialis electromyography, and electrocardiography. Respiratory inductance plethysmography was used to monitor respiratory effort during thoracoabdominal movement. Airflow was assessed using oronasal thermal and pressure sensors. A finger pulse oximeter was used to record oxygen saturation.

Sleep stages were identified based on the 2017 American Academy of Sleep Medicine criteria.<sup>16</sup> Apnea was defined as an airflow reduction  $> 90\%$  for  $\geq 10$ s relative to the pre-event baseline, and hypopnea was defined as a reduction in airflow  $\geq 30\%$  for  $\geq 10$ s relative to the pre-event baseline with  $\geq 3\%$  oxygen desaturation. OSA and CSA events were defined as apnea in the presence and absence of respiratory effort, respectively. Indexes of respiratory events were determined, including the central apnea index (CAI), obstructive apnea index (OAI), and mixed apnea index (MAI). A CAI/apnea-hypopnea index (AHI) ratio  $> 50\%$  is taken to indicate “true CSA”, while a CAI/AHI ratio  $\leq 50\%$  is defined as “companion CSA”. The oxygen desaturation index (ODI) was defined as the number of occasions on which the oxygen saturation decreased by  $3\%/h$ .

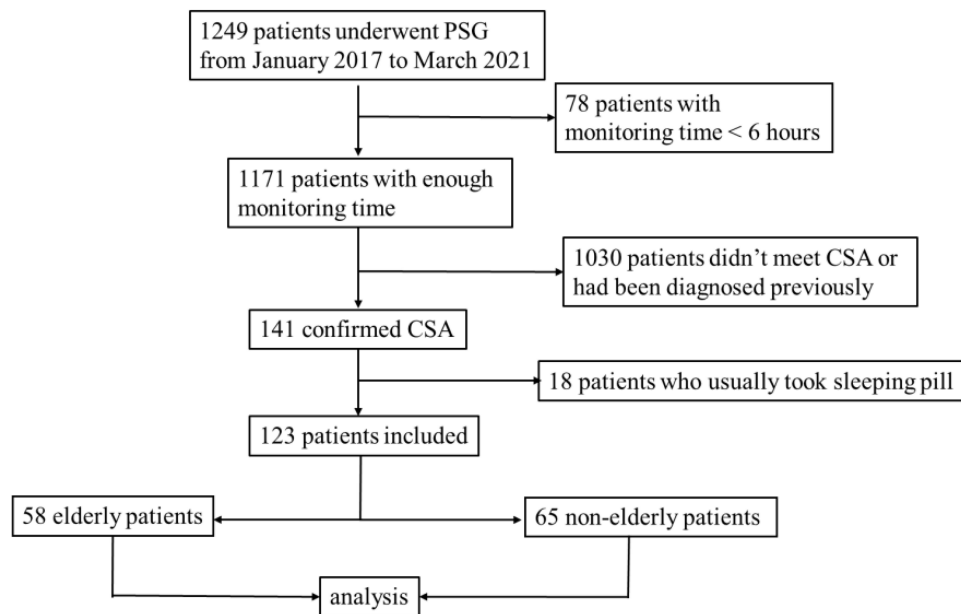
### Statistical Analysis

Quantitative data that conformed to a normal distribution were presented as mean  $\pm$  standard deviation (SD), while non-normally distributed parameters were described as median (P25, P75). Qualitative data were described as  $n$  (%). Between-group comparisons were conducted using the Independent Samples *t*-test, Mann–Whitney *U*-test, or chi-square test depending on the data type and normality of the data distribution. Multiple linear regression analysis was performed to assess the underlying factors of CAI. CAI was set as the dependent variable, and non-collinearity factors of polysomnography parameters, demographic characteristics, and comorbidities were set as independent variables in the multiple regression model. For all analyses, a two-tailed  $P < 0.05$  was considered significant. All analyses were performed using SPSS software (ver. 25; IBM Corp, Armonk, NY, USA).

## Results

### Demographic Characteristics and Comorbidities

123 out of 1249 patients were selected according to the inclusion and exclusion criteria and were divided into elderly ( $n = 58$ ) and non-elderly ( $n = 65$ ) groups (As shown in Figure 1). Both groups mainly comprised males, and there was no



**Figure 1** Cohort selection protocol.

difference in gender distribution between the two groups. BMI and waist circumference were significantly lower in the elderly group ( $P < 0.05$ ), while the elderly group had significantly higher rates of coronary heart disease, arrhythmias, and diabetes than the non-elderly group (Table 1).

## PSG Parameters and CSA Phenotype

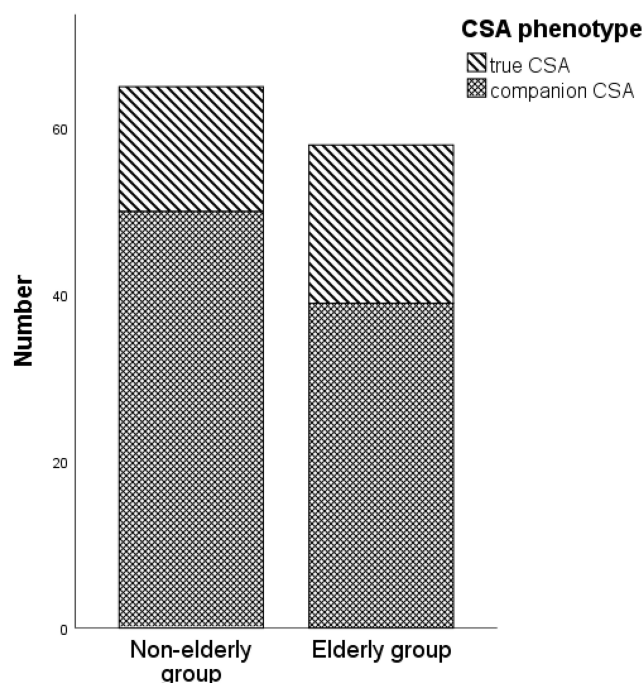
According to the definition of CSA in the Method-PSG monitoring section, companion CSA was more common than true CSA in both groups. The proportion of true CSA was higher in our elderly group, but there was no significant difference in the distribution of the different types of CSA between the two groups ( $\chi^2 = 1.436$ ,  $P = 0.231$ ) (Figure 2).

**Table 1** Demographic Characteristics and Comorbidities of the Elderly and Non-Elderly Groups

Parameters	Elderly <i>n</i> = 58	Non-elderly <i>n</i> = 65	$T/\chi^2$	<i>P</i>
<b>Demographic characteristics</b>				
Age, mean $\pm$ SD	72.26 $\pm$ 7.14	53.25 $\pm$ 7.97	17.220	<0.001***
Males, <i>n</i> (%)	46 (79.3%)	57 (87.7%)	1.582	0.209
<b>Anatomical characteristics (mean<math>\pm</math>SD)</b>				
BMI (kg/m <sup>2</sup> )	27.79 $\pm$ 3.67	29.79 $\pm$ 4.46	2.703	0.008**
Neck circumference (cm)	42.17 $\pm$ 3.47	42.72 $\pm$ 3.30	0.902	0.369
Waist circumference (cm)	103.19 $\pm$ 10.53	108.23 $\pm$ 12.29	2.428	0.017*
<b>Comorbidities, <i>n</i> (%)</b>				
Hypertension	33 (56.9%)	29 (44.6%)	1.849	0.174
Coronary heart disease	30 (51.7%)	13 (20.0%)	13.566	<0.001***
Arrhythmias	19 (32.8%)	7 (10.8%)	8.891	0.003**
Heart failure	3 (5.2%)	4 (6.2%)	0.550	0.815
Diabetes	12 (21.1%)	3 (4.6%)	7.609	0.006**
Cerebrovascular disease	2 (3.4%)	0 (0.0%)	2.278	0.131

**Notes:** \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$  vs the non-elderly group.

**Abbreviations:** SD, standard deviation; BMI, body mass index (weight in kilograms divided by the square of the height in meters).



**Figure 2** CSA often coexisted with other types of apnea (companion CSA). True CSA (CAI  $\geq 5$  and CAI/AHI ratio  $> 50\%$ ) was less common than companion CSA in both groups. Although true CSA tended to be more common in the elderly group, the difference was not significant.

The AHI (44.55 [33.23, 58.15] vs 55.10 [42.60, 71.40],  $P = 0.002$ ) and OAI (14.30 [7.70, 26.47] vs 24.40 [13.00, 43.00],  $P = 0.004$ ) of the elderly group were significantly lower than those of the non-elderly group. There was a trend toward a higher CAI in the elderly group (9.20 [6.90, 20.58] vs 8.70 [6.20, 17.00],  $P > 0.05$ ). To further measure the weight of central apnea in all apnea events, we calculated the ratio of CAI, MAI, and OAI to AHI, respectively. The ratio of CAI to AHI in the elderly group was significantly higher than that in the non-elderly group (0.264 [0.159, 0.474] vs 0.154 [0.109, 0.326],  $P = 0.003$ ). When discussing the desaturation during the period of sleep apnea, the ODI of the elderly group was lower than that of the non-elderly group (32.70 [19.30, 46.40] vs 45.30 [34.20, 60.20],  $P = 0.001$ ), and the lowest pulse oxygen saturation (LowSpO<sub>2</sub>) was higher in the elderly group (78.00 [71.00, 83.00] vs 73.00 [64.00, 80.00],  $P = 0.027$ ) (Table 2).

**Table 2** PSG Parameters of the Elderly and Non-Elderly Groups

Parameters <sup>a</sup>	Elderly n = 58	Non-elderly n = 65	Z	P
AHI (times/h)	44.55 [33.23, 58.15]	55.10 [42.60, 71.40]	3.086	0.002**
OAI (times/h)	14.30 [7.70, 26.47]	24.40 [13.00, 43.00]	2.893	0.004**
CAI (times/h)	9.20 [6.90, 20.58]	8.70 [6.20, 17.00]	0.722	0.470
MAI (times/h)	2.55 [0.90, 11.85]	3.80 [1.60, 14.20]	1.087	0.277
OAI/AHI	0.390 [0.169, 0.580]	0.661 [0.461, 0.753]	1.895	0.058
CAI/AHI	0.264 [0.159, 0.474]	0.154 [0.109, 0.326]	2.954	0.003**
MAI/AHI	0.078 [0.025, 0.219]	0.077 [0.032, 0.245]	0.372	0.710
MeanSpO <sub>2</sub> (%)	93.00 [90.80, 94.00]	93.00 [91.10, 94.20]	0.077	0.939
LowSpO <sub>2</sub> (%)	78.00 [71.00, 83.00]	73.00 [64.00, 80.00]	2.205	0.027*
ODI (times/h)	32.70 [19.30, 46.40]	45.30 [34.20, 60.20]	3.479	0.001**

**Notes:** <sup>a</sup>Parameters were presented as median (P25, P75); \* $P < 0.05$ , \*\* $P < 0.01$  vs the non-elderly group.

**Abbreviations:** AHI, apnea hypopnea index; OAI, obstructive apnea index; CAI, central apnea index; MAI, mixed apnea index; SpO<sub>2</sub>, pulse oxygen saturation; ODI, oxygen desaturation index.

**Table 3** Multiple Linear Regression Analysis for Central Apnea Index

	$\beta$	P	R <sup>2</sup>	P-value of the Mode
Age	0.256	0.005**	0.391	P<0.001
Males	0.022	0.792		
BMI	0.079	0.399		
OAI	-0.543	<0.001***		
MAI	-0.267	0.005**		
ODI	0.538	<0.001***		
Hypertension	0.064	0.480		
Coronary heart disease	-0.133	0.131		
Arrhythmias	-0.001	0.989		
Heart failure	0.300	<0.001***		
Diabetes	-0.052	0.533		
Cerebrovascular disease	0.012	0.876		

Notes: \*\*P < 0.01, \*\*\*P < 0.001.

Abbreviations: BMI, body mass index (weight in kilograms divided by the square of the height in meters); OAI, obstructive apnea index; MAI, mixed apnea index; ODI, oxygen desaturation index.

## Underlying Risk Factors for CSA

To evaluate the underlying factors related to CAI, we performed a multiple linear regression analysis. CAI was the dependent variable, and factors that may be related to CAI were included in the regression model as independent variables. AHI was excluded because CAI was a component of AHI. Neck and waist circumference were excluded because of their collinearity with BMI. The results indicated that age ( $\beta=0.256$ ,  $P=0.005$ ), OAI ( $\beta=-0.543$ ,  $P<0.001$ ), MAI ( $\beta=-0.267$ ,  $P=0.005$ ), ODI ( $\beta=0.538$ ,  $P<0.001$ ), heart failure ( $\beta=0.300$ ,  $P<0.001$ ) might be the underlying factors contribute to CAI (Table 3).

## Discussion

We conducted a retrospective study to investigate the characteristics of elderly CSA patients. The results indicated that CSA patients in the elderly group were more likely to comorbid with coronary heart disease, arrhythmia, and diabetes. Whether in the elderly or non-elderly group, CSA rarely existed independently but often coexisted with other types, ultimately leading to sleep apnea events. BMI, AHI, OAI, and ODI were lower, while the CAI to AHI ratio was higher in the elderly group than in the non-elderly group. The result of multiple regression analysis indicated age might be a potential risk factor for CAI.

In CSA, the cessation of oral and nasal airflow, as well as chest and abdominal breathing during sleep apnea, leads to hypoxemia, hypercapnia, and fragmented sleep, resulting in a series of pathological and physiological changes. CSA is subdivided into primary CSA, CSA with Cheyne Stokes breathing, CSA caused by disease without Cheyne Stokes breathing, and CSA caused by high-altitude periodic breathing, etc.<sup>17</sup> The pathogenesis varies among the different types of CSA, but they share a common pathological and physiological basis: periodic low or excessive ventilation leads to hypocapnia below the apnea threshold and a weaker central respiratory impulse, and high loop gain causes patients to experience periodic apnea.<sup>18,19</sup> Elderly people have impaired pharyngeal muscle tone, decreased local reflex activity in the pharyngeal cavity, more frequent brief awakenings, less stable sleep, and unstable respiratory regulation function. The proportion of elderly people taking oral psychotropic drugs,<sup>12</sup> concomitant cardiovascular and cerebrovascular diseases has increased, in turn greatly increasing the incidence of CSA.<sup>11,20</sup> Night-time apnea in elderly individuals may not be apparent, and memory loss and cognitive function changes are also easily misdiagnosed as age-related degenerative changes. Clinical features often overlap with underlying disorders.<sup>21</sup> Therefore, understanding the characteristics of CSA in elderly patients is of great importance for early identification and management of the disease.

In this study, there were significantly more male CSA patients than females in both the elderly and non-elderly groups and the BMI was lower in the elderly group. Lucas et al reported that the overall prevalence of CSA in a community population was 0.9%, with incidence rates of CSA in men and men aged > 65 years of 1.8% and 2.7%, respectively.<sup>22</sup>

Similarly, Bixler et al reported that CSA was significantly more prevalent among males than females.<sup>23</sup> A recent investigation showed obesity prevalence was 39.8% among US adults aged 20–39 years, 44.3% among adults aged 40–59 years, and 41.5% among adults aged 60 years and older.<sup>24</sup> These data are consistent with our results, that is BMI is lower in the elderly group. Evidence shows that the prevalence of OSA increases in individuals with obesity,<sup>25</sup> on the other hand, weight loss is associated with a significant improvement in the severity of OSA.<sup>26</sup> The lower BMI may be part of the reasons for the lower OAI in the elderly group in our study.

Inflammation, oxidative stress, and hypoxia are reported as key mediators that link OSA with various comorbidities, such as obesity, cardiovascular disease, and diabetes. Chronic intermittent hypoxia, the hallmark of OSA, leads to endothelial dysfunction and the progression of atherosclerosis, then increases the risk of hypertension, stroke, and myocardial infarction.<sup>27–29</sup> However, the association between these comorbidities and CSA is rarely reported in the literature. In our study, the proportions of elderly participants with coronary heart disease, and diabetes were significantly higher than those of the non-elderly participants. This result seems to contrast with the established associations between OSA and coronary heart disease, and diabetes. This inconsistency may reflect the important role of age in diabetes and coronary heart disease morbidity.

It is widely believed that CSA is closely related to arrhythmia and heart failure.<sup>21,30–34</sup> We speculate that the small sample size for heart failure cases may have limited our ability to detect statistically significant differences between the two groups. However, heart failure was independently associated with CAI when a multiple regression was conducted. Although the proportion of patients with arrhythmia was higher in the elderly group, unfortunately, our multiple analyses did not confirm the correlation between arrhythmia and CSA. Studies involving multiple centers and a large sample size are required to obtain higher-level evidence.

CAI in the elderly group showed a trend higher than that in the non-elderly group with no statistical difference, however, the ratio of CAI to AHI was significantly higher in the elderly group. Besides, the result of multiple regression analysis supported that CAI was positively correlated with age. The above results indicated that elderly patients had a potentially higher risk of developing CSA. Whether in the elderly or non-elderly group, CSA rarely existed independently but coexisted with other types, ultimately leading to sleep apnea events, which was consistent with our previous results.<sup>35</sup> True CSA seemed more common in our elderly group.

Compared to the non-elderly group, the elderly group had lower ODI and higher lowest SpO<sub>2</sub>, indicating a milder decrease in blood oxygen saturation in elderly patients during sleep apnea events. This may be related to the lower rate of OSA events in elderly patients. In clinical practice, we found that the severity of intermittent hypoxia was greater in OSA than in CSA. No relevant literature was found on the comparison of blood oxygen saturation between OSA and CSA. We speculate that, during CSA, the airway is not completely blocked, and air may enter the lungs through the still-open airway for gas exchange. When OSA occurs, the airway is blocked and no air enters the lungs.

There were limitations in this study. This was a single-center retrospective study with a relatively small sample size, thus we could only investigate the differences between the elderly and non-elderly patients with CSA, but not draw a causal relationship. When determining the patients' comorbidities, we could only rely on the medical records. Some information was not available. Due to strict selection criteria, the sample size was relatively small. This might limit the ability to detect statistically significant associations with certain indicators, such as heart failure. Nevertheless, as far as we knew, this was one of the only studies to explore the clinical characteristics of elderly CSA patients, and the results might improve the understanding and attention of CSA.

## Conclusion

In summary, CSA typically coexists with other types of sleep apnea. Elderly CSA patients has characteristics such as a milder decrease in blood oxygen saturation, combined with arrhythmia and coronary heart disease. Age may be a potential risk factor for CSA.

## Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.





## Ethical Statements

This study was approved by the Ethics Committee of the Tianjin Chest Hospital (2024LW-030). All the scientific research processes and data were supervised by the hospital ethics committee.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that no conflicting financial interests exist.

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