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Original Research

Correlation between Obstructive Sleep Apnea Syndrome (OSAS) and Cognitive Dysfunction in Elderly Patients with Hypertension

Wei Xia[1,*], Yongle Jing[1], Chao Yuan[1]

[1]Department of Cardiology, Tianjin First Central Hospital, 300192 Tianjin, China
*Correspondence: xiaweidoctor@yeah.net (Wei Xia)

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Abstract

Introduction: Obstructive sleep apnea syndrome (OSAS) is a common clinical disease that seriously affects the quality of life and health of patients. This study aimed to explore the correlation between OSAS and cognitive dysfunction in elderly patients with hypertension. **Methods**: A total of 106 elderly hypertensive patients were included and divided into OSAS group (n = 45) and non-OSAS group (n = 61), according to whether they combined with OSAS. OSAS was monitored with a portable polysomnography monitor by monitoring sleep and breathing. The cognitive dysfunction of the patients was evaluated using the Montreal Cognitive Assessment (MoCA). Basic data and MoCA scores of the patients were compared between the OSAS group and non-OSAS group. The correlation between OSAS and cognitive dysfunction in patients was evaluated using Pearson's correlation analysis. **Results**: The proportion of men (38 *vs.* 22, $p = 0.000$), atrial fibrillation (31 *vs.* 19, $p = 0.000$), body mass index (27.32 $\pm$ 3.85 *vs.* 21.27 $\pm$ 5.90, $p = 0.002$), systolic pressure (167.76 $\pm$ 14.31 *vs.* 153.22 $\pm$ 12.79, $p = 0.008$), homocysteine (29.71 $\pm$ 6.27 *vs.* 12.50 $\pm$ 4.19, $p = 0.005$), cognitive dysfunction (15 *vs.* 10, $p = 0.042$) in patients of the OSAS group were significantly higher compared to patients of the non-OSAS group. Visual space/executive ability (3.12 $\pm$ 1.23 *vs.* 4.75 $\pm$ 1.03, $p = 0.021$), memory (2.48 $\pm$ 0.31 *vs.* 3.71 $\pm$ 0.42, $p = 0.039$), attention (4.15 $\pm$ 1.21 *vs.* 5.12 $\pm$ 1.87, $p = 0.041$), total MoCA scores (20.11 $\pm$ 5.09 *vs.* 25.76 $\pm$ 4.31, $p = 0.017$) in patients in the OSAS group were significantly lower compared to patients in the non-OSAS group. OSAS was positively correlated with cognitive dysfunction in elderly patients with hypertension ($r = 0.224$, $p < 0.05$). **Conclusions**: OSAS was positively correlated with cognitive dysfunction in elderly patients with hypertension, so OSAS could increase the risk of cognitive dysfunction through its own adverse effects or its accompanying disease status.

Keywords: hypertension; obstructive sleep apnea syndrome (OSAS); cognitive dysfunction; elderly patients with hypertension; correlation

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a common clinical disease that seriously affects the quality of life and health of patients [1,2]. Previous studies have shown that the incidence rate of OSAS increases significantly with age, and the prevalence of OSAS in the elderly over 65 years of age is as high as 20%–40% [3,4]. A study in Hong Kong, China, showed that the incidence rate of OSAS in elderly over 60 years was 63.7% [5]. Hypertension and OSAS interact and aggravate each other, with 50% of OSAS patients complicating hypertension, and at least 30% of hypertension patients complicating OSAS [6]. Therefore, OSAS has a high incidence rate in patients with hypertension, especially in elderly patients with hypertension [7]. Patients with OSAS are repeatedly awakened during sleep, resulting in interruption of sleep and fragmentation of sleep. Additionally, nocturnal hypoxemia and repeated wakefulness usually lead to daytime sleepiness and cognitive impairment. The purpose of this study is to find out the risk factors of OSAS in cognitive dysfunction in elderly patients with hypertension to prevent and treat cognitive dysfunction in elderly patients with hypertension and improve their quality of life.

2. Materials and Methods

2.1 Subjects

This study included 106 elderly patients with hypertension hospitalized in the Department of Cardiology of Tianjin First Central Hospital from June 2017 to June 2020, including 60 male patients and 46 female patients, aged 60 to 77 (69.45 $\pm$ 5.71) years. These patients were divided into the OSAS group (n = 45) and the non-OSAS group (n = 61), depending on whether they were combined with OSAS. Body mass index (BMI), systolic blood pressure, diastolic blood pressure, cases of coronary heart disease, cases of atrial fibrillation, and cases of diabetes mellitus. The information was listed in Table 1. This study should be in accordance with the following inclusive criteria: ① Patients were over 60 years old (>60 years); ② Patients met the diagnostic criteria for hypertension; ③ Patients were in good compliance and voluntarily signed informed consent. This study also met the following exclusive criteria: ① Patients had incomplete clinical data; ② Patients currently received OSAS treatment; ③ Patients had neurolog-

ical or psychiatric diseases that affected cognitive function; ④ Patients had received any drug treatment affecting cognitive function 3 months before enrollment.

Table 1. Basic characteristics of elderly patients with hypertension.

Characteristics	Values
Cases (n)	106
OSAS	45
non-OSAS	61
Gender (n)	106
Male	60
Female	46
Age [year, (mean ± SD)]	69.45 ± 5.71
Systolic pressure (mmHg, mean ± SD)	160.49 ± 13.55
Diastolic pressure (mmHg, mean ± SD)	70.81 ± 14.08
Coronary heart disease [cases (%)]	48 (45.3)
Atrial fibrillation [cases (%)]	50 (47.2)
Diabetes mellitus [cases (%)]	62 (58.5)

OSAS, Obstructive sleep apnea syndrome.

This study has been approved by the Ethics Committee of Tianjin First Central Hospital (approval No. 2020N173KY). All patients have provided the written formed consents and approved this study.

2.2 OSAS Monitor

On day of monitoring, patients were prohibited to drink alcohol or coffee and stop sedative hypnotics and muscle relaxants. A portable polysomnography monitor (YH1000, Compumedics, Abbotsford, Victoria, Australia) was used to monitor sleep and breathing of patients. The entire monitoring process was completed in the sleep breathing monitoring room. Sleep breathing at night was monitored for not less than 7 h, and respiratory airflow from the mouth and nose, snoring and hypopnea index of apnea (the sum of the average number of apnea and hypopnea per hour was the hypopnea index of apnea) and blood oxygen saturation were recorded. The diagnostic criteria for OSAS referred to the Guidelines for the diagnosis and treatment of obstructive sleep apnea hypopnea syndrome (2011 Revision) [8]: adults have recurrent episodes of apnea and hypopnea more than 30 times during 7 h night sleep, or apnea hypopnea index $\geq$5 times/h.

2.3 Cognitive Dysfunction Evaluation

The cognitive dysfunction of the patients was evaluated using the Montreal Cognitive Assessment (MoCA), according to a previously published study [9] with a few modifications. Briefly, from 19:00 to 20:00 on the day of enrollment, MoCA was used to evaluate the cognitive functions of patients, including visual space/executive ability, naming ability, memory, attention, language ability, abstraction ability, and directional ability. If the patients have less than 12 years of education, the total score of MoCA should be increased by 1 point to correct the deviation. The MoCA score range is 0–30 points, and the normal value is more than 26 points ($\geq$26 points). The higher the score, the better the cognitive function. If the MoCA score is less than 26 ($<$26), it is determined that there is cognitive dysfunction. MoCA was carried out in this study was by professionals and completed alone and once every 10 min.

2.4 Data Collection

The basic data of the patients were collected in detail, including age, sex, body weight, height, coronary heart disease, atrial fibrillation, diabetes, blood lipids and homocysteine. 24 h ambulatory blood pressure monitoring was performed after admission and mean systolic pressure and diastolic blood pressure were measured. OSAS was recorded according to sleep monitoring results and the cognitive function of the patients was evaluated. The correlation between OSAS and cognitive dysfunction in elderly patients with hypertension was evaluated using Pearson's correlation analysis.

2.5 Statistical Analysis

In this study, SPSS statistical software (21.0, IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Measurement data were defined as mean ± standard deviation (SD), analyzed by Student's t test, while counting data was defined as percentage (%) and analyzed by the χ^2 test. Pearson's correlation analysis was used to analyze the correlation between OSAS and cognitive dysfunction in patients. $p < 0.05$ represented the statistical difference.

3. Results

3.1 Comparison of Clinical Data of Patients between OSAS and Non-OSAS Group

In this study, the OSAS patients were diagnosed according to the recurrent episodes of apnea and hypopnea more than 30 times during 7 h night sleep, or apnea hypopnea index. There were no significant differences in age, coronary heart disease, diabetes, diastolic blood pressure, and blood lipid levels between the two groups (Table 2, $p > 0.05$). The proportion of male gender (38 *vs.* 22, $p = 0.000$), atrial fibrillation (31 *vs.* 19, $p = 0.000$), body mass index (27.32 ± 3.85 *vs.* 21.27 ± 5.90, $p = 0.002$), systolic blood pressure (167.76 ± 14.31 *vs.* 153.22 ± 12.79, $p = 0.008$), homocysteine (29.71 ± 6.27 *vs.* 12.50 ± 4.19, $p = 0.005$) and cognitive dysfunction (15 *vs.* 10, $p = 0.042$) in patients of the OSAS group were significantly higher compared to those of the non-OSAS group (Table 2). Therefore, male gender, atrial fibrillation, body mass index, systolic blood pressure, homocysteine, and cognitive dysfunction were risk factors for OSAS in elderly patients with hypertension.

Table 2. Comparison of the general clinical data of the patients between the OSAS group and the non-OSAS groups.

Characteristics	OSAS group (n = 45)	non-OSAS group (n = 61)	χ^2/t value	p value
Age (year, mean ± SD)	70.62 ± 5.90	68.27 ± 5.51	1.463	0.471
Male [cases (%)]	38 (84.4)	22 (36.1)	24.675	0.000
Coronary heart disease [cases (%)]	20 (44.4)	28 (45.9)	0.022	0.882
Atrial fibrillation [cases (%)]	31 (68.9)	19 (31.1)	14.802	0.000
Diabetes mellitus [cases (%)]	27 (60.0)	35 (57.4)	0.073	0.786
Body mass index (kg/m^2, mean ± SD)	27.32 ± 3.85	21.27 ± 5.90	4.453	0.002
Systolic pressure (mmHg, mean ± SD)	167.76 ± 14.31	153.22 ± 12.79	3.993	0.008
Diastolic pressure (mmHg, mean ± SD)	71.33 ± 15.36	70.29 ± 12.80	1.573	0.442
TC (mmol/L, mean ± SD)	5.32 ± 0.81	5.27 ± 0.93	1.296	0.427
TG (mmol/L, mean ± SD)	2.24 ± 0.63	2.35 ± 0.47	1.573	0.391
LDL-C (mmol/L, mean ± SD)	3.54 ± 0.73	3.49 ± 0.86	1.956	0.212
HDL-C (mmol/L, mean ± SD)	0.85 ± 0.21	0.80 ± 0.25	1.891	0.295
Homocysteine (µmol/L, mean ± SD)	29.71 ± 6.27	12.50 ± 4.19	4.001	0.005
Cognitive dysfunction [cases (%)]	15 (33.3)	10 (16.4)	4.123	0.042

OSAS, obstructive sleep apnea syndrome; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein-cholesterol.

3.2 Comparison of MoCA Scores of Patients between OSAS and the Non-OSAS Group

There were no significant differences for the ability to name, language ability, abstraction ability, and direction ability of the patients between the OSAS group and the non-OSAS group (Table 3, $p > 0.05$). Visual space/executive ability (3.12 ± 1.23 *vs.* 4.75 ± 1.03, $p = 0.021$), memory (2.48 ± 0.31 *vs.* 3.71 ± 0.42, $p = 0.039$), attention (4.15 ± 1.21 *vs.* 5.12 ± 1.87, $p = 0.041$), and total MoCA scores (20.11 ± 5.09 *vs.* 25.76 ± 4.31, $p = 0.017$) in patients in the OSAS group were significantly lower compared to those of patients in the non-OSAS group (Table 3). Thus, patients with OSAS demonstrated lower visual space/executive ability, memory, and attention, with impaired cognition.

3.3 OSAS was Positively Correlated with Cognitive Dysfunction in Elderly Patients with Hypertension

According to the above findings, the proportion of cognitive dysfunction in patients in the OSAS group was obviously higher compared to that of patients in the non-OSAS group. Therefore, this study used the Pearson's correlation analysis to evaluate the correlation between OSAS and cognitive dysfunction in patients. The results of the Pearson's correlation analysis showed that OSAS was positively correlated with cognitive dysfunction in elderly patients with hypertension ($r = 0.224$, $p < 0.05$).

4. Discussion

OSAS, as a common clinical disease, has a high incidence rate in elderly patients with hypertension [10]. The results of sleep breathing monitoring in 106 elderly patients with hypertension showed that up to 42.5% of elderly patients with hypertension were complicated with OSAS. A previous study [11] focusing on OSAS has shown that in addition to impaired systemic system functions, cognitive dysfunction is the main neurological complication of OSAS. This study showed that the proportion of patients with cognitive dysfunction in patients in the OSAS group was significantly higher compared to that in patients in the non-OSAS group. Pearson's correlation analysis showed that OSAS was positively correlated with cognitive dysfunction in elderly patients with hypertension. This study demonstrated that the effect of OSAS on cognitive dysfunction in elderly patients with hypertension was manifested mainly in visual space/executive ability, memory and attention, showing a significant statistical difference compared to the patients in the non-OSAS group, which is consistent with previous research results [12]. The decrease in nocturnal blood oxygen saturation in OSAS patients can cause intermittent hypoxia in the hippocampus and cerebral cortex, resulting in metabolic abnormalities and cognitive damage [13]. OSAS patients are repeatedly awakened during sleep, resulting in sleep interruption and sleep fragmentation [14]. Some scholars believe that OSAS patients' cognitive function is affected by sleep structure disorders such as increased light sleep, decreased deep sleep and rapid-eye-movement (REM) sleep [15]. It is also believed that nocturnal hypoxemia caused by OSAS affects cognitive function [16]. Therefore, poor sleep quality at night is also the cause of daytime sleepiness and cognitive dysfunction.

Hypertension and OSAS interact and aggravate each other [17]. This study also showed that the systolic blood pressure level in patients in the OSAS group was significantly higher than in patients in the non-OSAS group. Hypertension is a risk factor for cardiovascular disease [18]. Elderly patients with hypertension have a certain degree of impact on cognitive function due to their own degenerative diseases of the cerebrovascular system. At the same time,

Table 3. Comparison of the MoCA scores of the patients between the OSAS group and the non-OSAS groups (mean ± SD).

Characteristics	OSAS group (n = 45)	non-OSAS group (n = 61)	*t* value	*p* value
Visual space/Executive ability	3.12 ± 1.23	4.75 ± 1.03	2.196	0.021
Naming ability	2.20 ± 0.76	2.35 ± 0.69	0.652	0.432
Memory	2.48 ± 0.31	3.71 ± 0.42	2.147	0.039
Attention	4.15 ± 1.21	5.12 ± 1.87	2.082	0.041
Language ability	1.30 ± 0.74	1.35 ± 0.89	0.541	0.661
Abstraction ability	1.16 ± 0.62	1.37 ± 0.45	0.591	0.504
Directional ability	4.72 ± 1.22	4.96 ± 1.17	0.367	0.730
Total score	20.11 ± 5.09	25.76 ± 4.31	3.097	0.017

MoCA, Montreal Cognitive Assessment.

combined with the previous impact of OSAS on blood pressure and cognitive function, elderly patients with hypertension and OSAS have a higher risk of cognitive impairment [19].

There are plenty of literatures [20,21] that indicate the OSAS patients (or hypertension patients) can manifest the neurocognitive deficits. Meanwhile, the OSAS patients present several comorbidities, such as the obesity, diabetes, and hypertension, all of which are associated with the cognitive deficit [22]. However, Borges *et al*. [23] reported that OSAS patients without the comorbidities didn't lead to the cognitive impairment. Therefore, there is a debate in literature regarding to the effects of comorbidities related to the OSAS on cognitive deficits manifested by OSAS patients. Difference from the above documents, the findings of the present study proved that OSAS may increase the cognitive deficits in elderly hypertension patients by itself directly, or by combining with the accompanying diseases indirectly. According to our findings, as a curable disease, OSAS should be actively screened and treated in elderly hypertensive patients to reduce the risk of cognitive dysfunction in elderly hypertensive patients.

This study showed that the body mass index and the level of homocysteine in patients in the OSAS group were significantly higher compared to those in patients in the non-OSAS group, and both were also risk factors for cardiovascular and cerebrovascular diseases. A previous study [24] reported that with increasing body mass index, the incidence of cognitive dysfunction also gradually increases. The reason is that with an increase in body mass index, the risk of severe OSAS increases and difficulty of controlling blood pressure also increases, leading to insufficient cerebral perfusion and increased hypoxia in brain tissue, thus exacerbating the risk of cognitive dysfunction. Price *et al*. [25] reported that hyperhomocysteinemia was a high risk factor for cognitive dysfunction. Hyperhomocysteinemia can promote the appearance of atherosclerosis, cause leukoaraiosis, and brain atrophy, resulting in cognitive dysfunction [26]. Furthermore, hyperhomocysteinemia affects lipid metabolism, produces homocysteine thiolactone, and causes the death of neurons in the hippocampus, while region has mainly memory and spatial localization effects. Furthermore, our findings showed that the proportion of atrial fibrillation in patients in the OSAS group was significantly higher compared to those in patients in the non-OSAS group. The increase in the proportion of atrial fibrillation could be another reason for the high proportion of patients with cognitive dysfunction in the OSAS group. Many studies [27–29] have shown that atrial fibrillation was closely related to cognitive dysfunction and the mechanism could be related to the increased risk of cardiogenic ischemic stroke and cerebral microbleeds in patients with atrial fibrillation.

There are also some limitations in this study. First, the bias in case selection and the small number of samples. Second, the course of the patients involved was different. Third, the results of parameters linked to OSAS (such as apnea-hypopnea index (AHI), blood oxygen saturation (SaO_2)) were only analyzed by professional doctors and only the final results are provided to judge whether the patient has OSAS, however the detailed comparisons between both groups haven't been carried out. Fourth, the educational levels and sleepiness have not been detected in both elderly hypertension patients with and without OSAS. Fifth, some of the statistical analysis was not sufficient due to the limited data analysis capability of our team, and it would be better to apply the additional statistical methods to analyze the differences of parameters between groups. Sixth, the OSAS associated parameters linked to hypertension have not been specified, because this study mainly focused on correlation between OSAS and cognitive dysfunction in elderly hypertension patients and the previously documents reported associations between OSAS and hypertension. Seventh, OSAS was diagnosed due to recurrent episodes of apnea and hypopnea more than 30 times during 7 h night sleep or apnea hypopnea index, and the polysomnography (PSG) hasn't been evaluated in elderly hypertension patients with or without OSAS. With the increasingly serious aging in China, elderly patients with hypertension and patients with cognitive dysfunction are increasing. Large-scale clinical and basic research is necessary to explore the pathogenesis, brain imaging characteristics, clinical manifestations, and effective measures of prevention and treatment of cognitive dysfunction in el-

derly patients with hypertension and OSAS. Moreover, we would conduct the polysomnographic evaluations (such as electroencephalogram (EEG), eye movement electrooculogram (EOG), muscle or bone movement electromyography (EMG), heart rate electrocardiogram (ECG)) in further study.

5. Conclusions

In conclusion, OSAS was positively correlated with cognitive dysfunction in elderly patients with hypertension, so OSAS could increase the risk of cognitive dysfunction in elderly patients with hypertension through its own adverse effects or its accompanying disease status. This study would lay a theoretical foundation for the pathogenesis of cognitive dysfunction in elderly patients with hypertensive OSAS.

Abbreviations

OSAS, obstructive sleep apnea syndrome; MoCA, montreal cognitive assessment; BMI, body mass index.

Availability of Data and Materials

The data sets supporting the conclusion of this study are included in this article.

Author Contributions

WX designed this study, performed experiments and tests, analyzed the data, wrote the manuscript, and made critical corrections. YJ and CY carried out experiments and tests, conducting the literature review. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study has been approved by the Ethics Committee of Tianjin First Central Hospital (approval No. 2020N173KY). All patients have provided the written formed consents and approved this study.

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Conflict of Interest

The authors declare no conflict of interest.

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