• Brief Report •

Correlation between obstructive sleep apnea and central retinal vein occlusion

Yan-Hui Wang[1], Peng Zhang[2], Lian Chen[2], Zhao Jiang[2], Lu-Xi Li[2], Ke He[2], Xiao-Qing Li[2]

[1]Department of Otolaryngology, Xi'an No.3 Hospital, the Affiliated Hospital of Northwest University, Xi'an 710018, Shaanxi Province, China

[2]Department of Ophthalmology, Xi'an No.3 Hospital, the Affiliated Hospital of Northwest University, Xi'an 710018, Shaanxi Province, China

Correspondence to: Peng Zhang. Department of Ophthalmology, Xi'an No.3 Hospital, the Affiliated Hospital of Northwest University, the Third Fengcheng Road, Xi'an 710018, Shaanxi Province, China. zhangpengfmmu@163.com

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Abstract

• To investigate the possible correlation between obstructive sleep apnea (OSA) and central retinal vein occlusion (CRVO). Thirty consecutive patients with a recent (<3mo) CRVO and an age- and sex-matched group of 30 control subjects were recruited. All subjects underwent full-night polysomnography to measure apnea-hypopnea index (AHI) and oxygen desaturation index (ODI). The average AHI and ODI were significantly higher in CRVO patients (AHI: 13.86±8.63, ODI: 9.21±4.47) than in control subjects (AHI: 8.51±6.36, ODI: 5.87±3.18; *P*=0.008 and 0.001 respectively). Additionally, the AHI was positively correlated with body mass index (BMI; *r*=0.476, *P*=0.017) and ODI (*r*=0.921, *P*<0.01) in both CRVO and control subjects. According to AHI scores, twenty-two (73.33%) CRVO patients had OSA and 12 (40.00%) control subjects had OSA, a difference that was statistically significant (*P*=0.019). OSA may be a risk factor for or a trigger of CRVO development.

• KEYWORDS: central retinal vein occlusion; obstructive sleep apnea; polysomnography; apnea-hypopnea index; oxygen desaturation index

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INTRODUCTION

Central retinal vein occlusion (CRVO) is a common retinal vascular disorder that generally occurs in adults and can severely affect vision[1]. Histological studies have shown that thrombus formation within the central retinal vein lumen near the lamina cribrosa is the main cause of CRVO[1]. Thrombosis within a retinal vein leads to an increase in venous blood flow resistance, which causes circulatory stasis and a marked rise in retinal venous and capillary pressure[2].

Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder and is characterized by repeated episodes of upper airway obstruction that result in apnea (breathing pause) and/or hypopnea (airflow reduction) during sleep[3-4]. The subsequent reduction in alveolar ventilation causes a decrease in oxygen saturation and, potentially, an increase in carbon dioxide partial pressure, which may induce hypoxemia, hypercapnia and/or increased sympathetic activity[5]. The occurrence of OSA has been associated with several systemic diseases, including atherosclerosis, hypertension, diabetes mellitus, and stroke. These conditions are also risk factors for CRVO[2].

The current study prospectively examined OSA prevalence in subjects with and without CRVO and specifically assessed whether or not OSA is a risk factor for CRVO.

SUBJECTS AND METHODS

Ethical Approval This study followed tenets of the Declaration of Helsinki, with approval from the Ethics Committee at Xi'an No.3 Hospital. Informed consent was obtained from all subjects.

Subjects Patients with a recent (<3mo) CRVO were considered for study enrollment at Xi'an No.3 Hospital (Xi'an, China) between January 2017 and December 2018. Research volunteers without CRVO were also enrolled as a control group. Control subjects were age- and gender-matched by random sampling. Subjects with diabetes mellitus, stroke, coronary artery disease or other comorbidities reported to be associated with OSA were excluded, with the exception of subjects with well-controlled hypertension.

Methods The presence of a CRVO was confirmed by a retinal specialist with indirect ophthalmoscopy and fluorescein angiography (FA). Logarithm of the minimum angle of resolution (logMAR) best-corrected visual acuity (BCVA), intraocular pressure, and body mass index (BMI) were measured in all included subjects. All subjects underwent polysomnography using a commercially-available, portable

sleep monitor (Somté, Compumedics, Abbotsford, Australia). Sleep testing began at 23:00 and ended at 06:30. The apnea-hypopnea index (AHI), oxygen desaturation index (ODI) were recorded and compared.

The OSA severity was classified using the AHI score, which represents the number of apnea and hypopnea events per hour of sleep, into the following categories: normal (AHI<5), mild (5≤AHI≤14), moderate (15≤AHI≤30), and severe (AHI>30)[6]. Statistical analyses were conducted using SPSS statistical software (version20.0; SPSS Inc., Chicago, IL, USA). All data are presented as mean±standard deviation or *n* (%) as applicable. Comparisons between CRVO and control subjects were made using Pearson's Chi-square tests for categorical variables and independent Student's *t*-tests for continuous variables. Pearson's correlation analysis was also performed to assess relationships between CRVO and the presence of OSA. Statistical significance was defined as $P<0.05$.

RESULTS

This study included 30 subjects with CRVO and 30 age- and gender-matched controls. Average age of CRVO patients was 52.51±11.72y (range, 35 to 70y); the average age of control subjects was 50.79±12.43y (range, 36 to 71y). The demographic and polysomnographic data for CRVO group and controls are presented in Table 1. There were no statistical differences in age, sex, intraocular pressure and hypertension history between CRVO patients and control subjects. The differences of logMAR BCVA, BMI, AHI and ODI were statistically significant between CRVO patients and control subjects.

For all patients, AHI showed a positive correlation with BMI ($r=0.476$, $P=0.017$) and ODI ($r=0.921$, $P<0.001$). However, AHI had no significant correlation with age, IOP and logMAR BCVA. According to AHI score, 22 (73.33%) of 30 with CRVO patients had OSA; 12 (40.00%) of 30 control subjects had OSA. The prevalence of OSA was statistically different between CRVO patients and control subjects. Table 2 shows the comparison of OSA severity in CRVO patients and in control subjects.

Table 1 Demographic characteristics and polysomnographic data for patients with central retinal vein occlusion and control subjects mean±SD

Variables	CRVO group	Control group	*P*
Subjects (*n*)	30	30	-
Age (y)	52.51±11.72	50.79±12.43	0.583
Sex (female/male)	12/18	11/19	0.792
IOP (mm Hg)	14.42±5.71	15.17±5.02	0.591
HTN (yes/no)	13/17	10/20	0.595
BCVA, logMAR	0.45±0.47	0.72±0.53	0.041
BMI	26.87±4.45	24.64±3.46	0.033
AHI	13.86±8.63	8.51±6.36	0.008
ODI	9.21±4.47	5.87±3.18	0.001

CRVO: Central retinal vein occlusion; HTN: Hypertension; BCVA: Best-corrected visual acuity; logMAR: Logarithm of the minimum angle of resolution; IOP: Intraocular pressure; BMI: Body mass index; AHI: Apnea-hypopnea index; ODI: Oxygen desaturation index.

Table 2 Comparison of obstructive sleep apnea in patients with central retinal vein occlusion and in control subjects *n* (%)

OSA	CRVO group (*n*=30)	Control group (*n*=30)	*P*
Total	22 (73.33)	12 (40.00)	0.019
Mild	8 (26.67)	4 (13.33)	0.333
Moderate	9 (30.00)	6 (20.00)	0.551
Severe	5 (16.67)	2 (6.67)	0.421

CRVO: Central retinal vein occlusion; OSA: Obstructive sleep apnea.

DISCUSSION

The prevalence of OSA is approximately 4.8% in the Asian population, its incidence is expected to rise in an aging and obesity population[7]. OSA are usually insidious during sleep and most patients are unaware of experiencing OSA symptoms[5]. Polysomnography is a multi-parametric test used in the study of sleep and as a diagnostic tool in sleep medicine. According to AHI and oxygen desaturation levels recorded by overnight polysomnography monitoring, the severity of obstructive sleep apnea can be defined[8].

This study indicated that AHI and ODI scores were significantly higher in the CRVO patients (AHI: 13.86±8.63, ODI: 9.21±4.47) than in the control subjects (AHI: 8.51±6.36, ODI: 5.87±3.18; $P=0.008$ and 0.001 respectively). Correspondingly, the prevalence of OSA were significantly higher in CRVO patients (73.33%) than in control subjects (40.00%; $P=0.019$). Therefore, OSA may be a risk factor for CRVO development.

OSA is characterized by a marked sympathetic overdrive, which triggers cerebral blood flow velocity dramatically and oxygen saturation decrease[9]. These changes may increase intracranial pressure and venous pressure on the optic papillary, mechanically impeding retinal blood flow, reducing spontaneous venous pulsation, leading to an increase in retinal venous pressure[9-10].

AHI was correlated with the BMI, which corroborates the known association between OSA severity and excess body weight[11]. This study also confirmed this correlation in both CRVO and control subjects. Clinical observations have proven that excess weight is a well-established predictor of sleep-disordered breathing (SDB)[11]. Age and excess weight are also known as risk factors of diabetes mellitus, hypertension, and arteriosclerosis, which have been reported to be associated with CRVO[12]. Therefore, weight loss may benefit not only on OSA severity but also in mitigating systemic diseases related to both OSA and obesity.

Intermittent nocturnal hypoxemia is another characteristic of OSA[6]. The ODI can reflect intermittent nocturnal hypoxemia severity. Intermittent nocturnal hypoxia may increase systemic oxidative stress and produce reactive oxygen species and inflammatory cytokines, such as interleukin 1 (IL-1) and interleukin 6 (IL-6), which may activate the extrinsic coagulation pathway and subsequent venous thrombosis in OSA patients and trigger CRVO development[13-15].

Based on the high prevalence of OSA in CRVO patients in this study, we believe that OSA could be a risk factor for occurance of CRVO. In addition, OSA may function as a triggering factor for patients of CRVO with predisposing conditions, such as hypertension, diabetes mellitus, atherosclerosis[1]. We should pay attention to the role of OSA involving in pathogenesis of CRVO, and we suggest that diagnostic polysomnography should be considered as an appropriate adjunct for each CRVO patients other than diagnostic imaging of retina.

The main limitation of this study was its small sample size. Further studies are needed on a larger group of patients to confirm the high OSA incidence in CRVO patients and to understand if OSA treatment can influence CRVO development and/or regression.

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REFERENCES

1 Hayreh SS, Podhajsky PA, Zimmerman MB. Natural history of visual outcome in central retinal vein occlusion. *Ophthalmology* 2011;118(1):119-133.e1-2.

2 Koylu MT, Kucukevcilioglu M, Erdurman FC, Durukan AH, Sobacı G, Torun D, Tunca Y, Ayyildiz O. Association of retinal vein occlusion, homocysteine, and the thrombophilic mutations in a Turkish population: a case-control study. *Ophthalmic Genet* 2017;38(4):352-356.

3 Lippi G, Mattiuzzi C, Franchini M. Sleep apnea and venous thromboembolism. A systematic review. *Thromb Haemost* 2015;114(5):958-963.

4 Chami HA, Resnick HE, Quan SF, Gottlieb DJ. Association of incident cardiovascular disease with progression of sleep-disordered breathing. *Circulation* 2011;123(12):1280-1286.

5 Lombardi C, Tobaldini E, Montano N, Losurdo A, Parati G. Obstructive sleep apnea syndrome (OSAS) and cardiovascular system. *Med Lav* 2017;108(4):276-282.

6 Ruehland WR, Rochford PD, O'Donoghue FJ, Pierce RJ, Singh P, Thornton AT. The new AASM criteria for scoring hypopneas: impact on the apnea hypopnea index. *Sleep* 2009;32(2):150-157.

7 Pilakasiri A, Mahakit P. Prospective study of the prevalence and co-morbidities of obstructive sleep apnea in active-duty army personnel in the three southernmost provinces of Thailand using questionnaire screening. *Mil Med Res* 2018;5(1):39.

8 Khan A, Patel J, Sharma D, Riaz S, Demissie S, Szerszen A. Obstructive sleep apnea screening in patients with atrial fibrillation: missed opportunities for early diagnosis. *J Clin Med Res* 2019;11(1):21-25.

9 Grassi G, Seravalle G, Brambilla G, Buzzi S, Volpe M, Cesana F, Dell'oro R, Mancia G. Regional differences in sympathetic activation in lean and obese normotensive individuals with obstructive sleep apnoea. *J Hypertens* 2014;32(2):383-388.

10 Tong JY, Golzan M, Georgevsky D, Williamson JP, Graham SL, Farah CS, Fraser CL. Quantitative retinal vascular changes in obstructive sleep apnea. *Am J Ophthalmol* 2017;182:72-80.

11 Glicksman A, Hadjiyannakis S, Barrowman N, Walker S, Hoey L, Katz SL. Body fat distribution ratios and obstructive sleep apnea severity in youth with obesity. *J Clin Sleep Med* 2017;13(4):545-550.

12 Jehan S, Myers AK, Zizi F, Pandi-Perumal SR, Jean-Louis G, McFarlane SI. Obesity, obstructive sleep apnea and type 2 diabetes mellitus: Epidemiology and pathophysiologic insights. *Sleep Med Disord* 2018;2(3):52-58.

13 Yang JY, You B, Wang Q, Chan SY, Jonas JB, Wei WB. Retinal vessel oxygen saturation in healthy subjects and early branch retinal vein occlusion. *Int J Ophthalmol* 2017;10(2):267-270.

14 Ntalapascha M, Makris D, Kyparos A, Tsilioni I, Kostikas K, Gourgoulianis K, Kouretas D, Zakynthinos E. Oxidative stress in patients with obstructive sleep apnea syndrome. *Schlaf Atmung* 2013;17(2):549-555.

15 Sartori MT, Barbar S, Donà A, Piermarocchi S, Pilotto E, Saggiorato G, Prandoni P. Risk factors, antithrombotic treatment and outcome in retinal vein occlusion: an age-related prospective cohort study. *Eur J Haematol* 2013;90(5):426-433.