

# Obstructive Sleep Apnea and Venous Thrombosis: Clinical Implications

S Ramnathan Iyer<sup>1</sup>, Revati R Iyer<sup>2</sup>

## ABSTRACT

Obstructive sleep apnea (OSA), although a disease of upper respiratory airway, has profound effects on body systems. The breathing abnormalities have effects on venous return. Pooling of blood in legs during apnea-hypopnea, coupled with hemodynamic changes and pathological cascades, favors thrombosis in legs and subsequent thromboembolism. An OSA has possible implications in vascular endothelial injury, stagnant blood flow, increased coagulability (Virchow's triad), and Trousseau's syndrome. An OSA suspicion must be high in all patients with venous thrombosis, particularly in those who have recurrent episodes of this disorder.

**Keywords:** Obstructive sleep apnea, Venous return, Venous thromboembolism.

*Indian Journal of Sleep Medicine* (2020); 10.5005/jp-journals-10069-0057

## INTRODUCTION

Obstructive sleep apnea (OSA) has been recognized as a common and treatable disorder. It is characterized by repetitive pharyngeal collapse in sleep, which leads to cyclical hypoxia and cyclical sympathetic stimulation. These events pave the way for thrombosis. In fact, OSA has been labeled as a prothrombotic state. Thrombosis in the venous systems in patients with OSA is being increasingly recognized.

Venous return from legs is dependent upon the skeletal muscle pump, which is effective while the subject is walking. The changes in venous pressure coupled with normal functioning valves help the blood to go caudally. While standing, the postural muscles in legs alternately contract and relax to keep the body in balance. This muscle activity promotes venous return, maintains central venous pressure, lowers venous and capillary pressure in feet and lower limbs. Respiratory activity also contributes to venous return by the following mechanisms: (a) Increasing the rate and depth of respiration promotes venous return and therefore enhances the cardiac output. (b) Intrapleural pressure becomes more negative during inspiration, which leads to the expansion of lungs, cardiac chambers (right atrium and right ventricle), and superior and inferior vena cava. The resultant fall in the intravascular and intracardiac pressure leads to increased venous return, increased preload and increased stroke volume. During expiration, the opposite occurs.

## OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea, although a common disorder, often escapes clinical recognition due to poor awareness among society and health professionals. An OSA is characterized by repetitive pharyngeal collapse in sleep, leading to cyclical hypoxemia, cyclical hypertension, release of catecholamines, and stress hormones. An OSA can affect any system since oxygen is the basic nutrient of all cells. It is a chronic condition where nocturnal events occur night after night. The effects of intermittent hypoxia (akin to intermittent respiratory failure) and reoxygenation may provoke a number of pathological cascades that involve sympathetic overactivity, oxidative stress, endothelial dysfunction, increased oxidative vascular injury and systemic inflammation. These nocturnal events are believed to be mechanisms contributing independently to increased cardiometabolic risk.<sup>1</sup> Chief

<sup>1</sup>Ambika Clinics-Dombivli (East) Dist Thane and Kharghar, Navi Mumbai, Maharashtra, India. Godrej Memorial Hospital, Vikhroli (East), Mumbai, Maharashtra, India

<sup>2</sup>Ambika Clinics-Dombivli (East) Dist Thane and Kharghar, Navi Mumbai, Maharashtra, India

**Corresponding Author:** S Ramnathan Iyer, Ambika Clinics-Dombivli (East) Dist Thane and Kharghar, Navi Mumbai, Maharashtra, India. Godrej Memorial Hospital, Vikhroli (East), Mumbai, Maharashtra, India, Phone: +91 9820143970, e-mail: sramiyer@gmail.com

**How to cite this article:** Iyer SR, Iyer RR. Obstructive Sleep Apnea and Venous Thrombosis: Clinical Implications. *Indian J Sleep Med* 2020;15(3):51–53.

**Source of support:** Nil

**Conflict of interest:** None

metabolic effects include decreased insulin sensitivity and worsening of glucose tolerance. OSA is a risk factor for hypertension, diabetes, ischemic heart disease, stroke, dementia and others.<sup>2</sup> There is a high prevalence of sleep-disordered breathing in patients with congestive heart failure (CHF).<sup>3</sup> Studies have suggested that 40–50% of patients with CHF and left ventricular systolic dysfunction will have some form of sleep-disordered breathing, either obstructive or central sleep apnea.<sup>3</sup> The presence of SDB affects cardiac function and ejection fraction adversely.

## EFFECTS OF OBSTRUCTIVE SLEEP APNEA ON VENOUS SYSTEM

Sympathetic activation causes vasoconstriction. The apneas and hypopneas contribute to reduced venous flow and pooling of blood in legs. Both contribute to venous hypertension. The changes in pleural pressure that promote venous return are also absent in apneas and hypopneas.

## OBSTRUCTIVE SLEEP APNEA AND VENOUS THROMBOSIS

In a nationwide population-based cohort study, Peng et al.<sup>4</sup> stated that patients with OSA exhibit a higher risk of subsequent deep vein thrombosis and pulmonary embolism. The specific underlying



## OBSTRUCTIVE SLEEP APNEA AND PREGNANCY AND VENOUS SINUS THROMBOSIS

Pregnant women possessing craniofacial abnormalities in both bony and soft tissues are believed to be predisposed to sleep-disordered breathing (SDB). Weight gain and obesity are important risk factors for the development of SDB in pregnancy. Aggarwal et al.<sup>15</sup> reported that maternal morbidity in terms of preeclampsia and meconium-stained liquor was higher among snorers and SDB population of pregnant women. SDB has been proposed as a risk factor for adverse maternal–fetal outcomes, including pregnancy-induced hypertension and small for gestational age births. Venous sinus thrombosis in puerperium is possibly related to OSA.

## OBSTRUCTIVE SLEEP APNEA AND RETINAL VEIN OCCLUSION

Glacet-Bernard et al.<sup>16</sup> found a higher-than-expected prevalence of OSA in a series of patients with retinal vein occlusion (RVO), suggesting that OSA could be an additional risk factor that plays an important role in the pathogenesis of RVO or at least that it is a frequently associated condition that could be a triggering factor. This association may explain why most patients discover visual loss on awakening.

## OBSTRUCTIVE SLEEP APNEA, CANCER AND VENOUS THROMBOSIS

Deep vein thrombosis and pulmonary embolism are the most common thrombotic conditions in patients with cancer. Nearly 15% of patients who develop deep venous thrombosis or pulmonary embolism have a diagnosis of cancer.<sup>17</sup> The coexistence of peripheral venous thrombosis/migratory thrombophlebitis with visceral carcinoma, particularly pancreatic cancer, is called Trousseau's syndrome. Rodriguez et al.<sup>18</sup> have reported increased overnight hypoxia, as a surrogate of OSA severity was associated with increased cancer incidence. This association seems to be limited to men and patients younger than 65 years of age.

Notwithstanding the potential limitations of the methodological approaches employed to date, the existing evidence strongly suggests that intermittent hypoxia and sleep fragmentation could play an important role in increasing cancer incidence and mortality in patients with sleep-disordered breathing, most likely by promoting sympathetic outflow, immunological alterations, or angiogenesis in the host response to tumor that ultimately results in markedly adverse tumor properties.<sup>19</sup>

The most common and accepted mode of therapy of OSA is the usage of continuous positive airway pressure while sleeping. This therapy has been found to be highly rewarding (opens the pharyngeal gate and closes the gates to various systemic disorders).

## CONCLUSION

There is a close relation between OSA and venous thrombosis. In a given clinical setting, it is important to recognize and treat this condition. The treatment of OSA by CPAP results in an overall improvement in all the consequences of OSA.

## REFERENCES

1. Somers VK, White DP, Amin R, et al. Sleep apnea and cardiovascular disease. An American Heart Association/American College Of Cardiology Foundation Scientific Statement from the American Heart

- Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council and Council on Cardiovascular Nursing. *J Am Coll Cardiol* 2008;52:696–717.
2. Iyer SR. Sleep and type II diabetes mellitus-its clinical implications. *J Assoc Physicians India* 2012;60:42–47.
3. Javaheri S, Parker TJ, Wexler L, et al. Occult sleep-disordered breathing in stable congestive heart failure [published erratum appears in *Ann Intern Med* 1995 Jul 1;123(1):77]. *Ann Intern Med* 1995;122(7):487–492. DOI: 10.7326/0003-4819-122-7-199504010-00002.
4. Peng YH, Liao WC, Chung WS, et al. Association between obstructive sleep apnea and deep vein thrombosis/pulmonary embolism. A population-based study. *Thromb Res* 2014;134(2):340–345. DOI: 10.1016/j.thromres.2014.06.009.
5. Yardim-Akaydin S, Caliskan-Can E, Firat H, et al. Influence of gender on C-reactive protein, fibrinogen and erythrocyte sedimentation rate in obstructive sleep apnea. *Antiinflamm Allergy Agents Med Chem* 2014;13(1):56–63. DOI: 10.2174/18715230113129990015.
6. Peled N, Kassirer M, Krammer MR, et al. Increased erythrocyte adhesiveness and aggregation in obstructive sleep apnea syndrome. *Thromb Res* 2008;121(5):631–636. DOI: 10.1016/j.thromres.2007.07.010.
7. Li KK, Kushida C, Powell NB, et al. Obstructive sleep apnea syndrome: a comparison between far east Asian and white men. *Laryngoscope* 2000;110(10 Pt 1):1689–1693. DOI: 10.1097/00005537-200010000-00022.
8. Alonso-Fernandez A, Suqula AG, Monica de la P, et al. OSA is a risk factor for VTE. *Chest* 2016;150(6):1291–1301. DOI: 10.1016/j.chest.2016.07.011.
9. Iyer SR, Iyer Revati R, Sonavdekar RB. Schamberg's disease in a case of severe obstructive sleep apnea: a case report. *Ind J Sleep Med* 2014;9(4):183–185. DOI: 10.5005/IJSM-9-4-183.
10. Duran J, Esnaola S, Rubio R, et al. Obstructive sleep apnea-hypopnea and related clinical features in a population based sample of subjects aged 30 to 70 years. *Am J Respir Crit Care Med* 2001;163(3 Pt 1):685–689. DOI: 10.1164/ajrccm.163.3.2005065.
11. Torbicki A, Ferrier A, Konstantinides S, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Heart J* 2008;29(18):2276–2315. DOI: 10.1093/eurheartj/ehn310.
12. Chou KT, Huang CC, Chen YM, et al. Sleep apnea and risk of deep vein thrombosis: a non randomized pair matched cohort study. *Am J Med* 2012;125(4):374–380. DOI: 10.1016/j.amjmed.2011.07.003.
13. Heit JA, Mohr DN, Silverstein MD, et al. Predictors of recurrence after deep vein thrombosis and pulmonary embolism: a population-based cohort study. *Arch Intern Med* 2000;160(6):761–768. DOI: 10.1001/archinte.160.6.761.
14. Iyer SR, Iyer RR, Bhagyalakshmi V. Avoiding type 2 diabetes express highway from infancy to old age-focus on newer risk factors. *J Assoc Physicians of India* 2019;67(1):68–72.
15. Aggarwal M, Suri JC, Suri S, et al. Maternal and fetal outcomes of sleep disordered breathing in pregnancy. *Indian J Sleep Med* 2008;3(1):25–29. DOI: 10.5005/ijsm-3-1-25.
16. Glacet-Bernard A, Jardine GLL, Lasry S, et al. Obstructive sleep apnea among patients with retinal vein occlusion. *Arch Ophthalmol* 2010;128(12):1533–1538. DOI: 10.1001/archophthalmol.2010.272.
17. Jameson JL, Longo DL. *Harrison's Principles of Internal Medicine*. 19th ed., Macgraw Hill, 2015. p. 613.
18. Rodriguez CF, MAM Garcia, Martinez M, et al. Association between obstructive sleep apnea and cancer. Incidence in large multicenter Spanish cohort. *Am J Respir Crit Care Med* 2013;187(1):99–105. DOI: 10.1164/rccm.201209-1671OC.
19. Gosal D, Farre R, Nieto JF. Obstructive sleep apnea and cancer: epidemiologic links and theoretical biological constructs. *Sleep Med Rev* 2016;27:43–55. DOI: 10.1016/j.smrv.2015.05.006.