REVIEW ARTICLE

Beyond the Breath: Exploring the Complex Nexus of Obstructive Sleep Apnea and Comorbid Conditions

Sanchit Mohan[1], Pranav Ish[2], Rohit Kumar[3], Nitesh Gupta[4], Vidushi Rathi[5], Nupoor Vaghasia[6]

Received on: 27 February 2024; *Accepted on:* 10 May 2024; *Published on:* 19 June 2024

Abstract

Obstructive sleep apnea (OSA) can have multi-system involvement, including cardiac, renal, pulmonary, neuropsychiatric, and endocrine complications. Several complications have shown a bidirectional relationship with OSA, and multiple mechanisms of bidirectional relationship have been studied in the literature, like fluid retention and redistribution in heart failure and renal and neural mechanisms in stroke and diabetes. The current review aims to explore comorbidities associated with OSA, look for bidirectional relationships, and the impact of therapy.

Keywords: Chronic respiratory failure, Metabolic syndrome, Obstructive sleep apnea, Overlap syndrome, Syndrome-Z.

Indian Journal of Sleep Medicine (2024): 10.5005/jp-journals-10069-0133

Introduction

Obstructive sleep apnea (OSA) is a type of sleep-disordered breathing (SDB) that is associated with increasing morbidity. Western data suggest an increase in the prevalence of OSA, that is, a mean of 22% in men and 17% in women.[1] As per the systematic review, the prevalence of OSA in India was 14% in males and 6% in females.[2] OSA is associated with multiple comorbidities, including metabolic, cardiovascular, pulmonary, neuropsychiatric, and renal. Among cardiovascular comorbidity, the strongest association lies between atrial fibrillation (AF) and hypertension.[3] Some of the comorbidities have a bidirectional relationship. As in heart failure (HF), fluid accumulation occurs in the neck in a recumbent position, resulting in OSA. Fluctuating intra-thoracic pressure, recurrent micro-arousals, and intermittent hypoxia leading to cellular and molecular consequences, including sympathetic excitation, systemic inflammation, and oxidative stress causing metabolic and endothelial dysfunction, are the possible mechanisms of OSA leading to various comorbidities.[4] It is important to suspect and diagnose OSA as patients usually present with comorbid conditions that are difficult to control, leading to morbidity; once OSA is treated, outcomes have improved.[5]

The current review explores the possible comorbidities associated with OSA, the bidirectional relationship, and the effect of therapy.

OSA and the Comorbidities

Impact on Cardiovascular Health

Heart Failure

Heart failure is usually associated with central sleep apnea (CSA). However, OSA is not uncommon. Risk factors of HF and OSA are common, such as age, high BMI, and sedentary lifestyle. Data from extensive epidemiological studies suggest an elevated risk of coronary artery disease (CAD), congestive heart failure, and cardiovascular comorbidities in patients with OSA.[6] A prospective study of OSA and incidence of CAD and HF showed that severe OSA (Apnea-hypopnea index [AHI] > 30) increases the risk of HF by 58%.[7]

An increase in the number of obstructive events leads to significant changes in intra-thoracic pressure, causing an increase in preload and a decrease in afterload due to reduced left ventricular filling pressures resulting in activation of renin-angiotensin activation system (RAAS), leading to sodium and water retention.[8] OSA causes cardiac remodeling, leading to diastolic dysfunction and heart failure.[9]

In a study by Schulz et al.[10] in 203 patients with HF with reduced ejection fraction (< 40%) showed 71% of patients had AHI >10 and 43% met diagnostic criteria of OSA.

Patients with HF promote fluid retention due to the triggering of neurogenic and humoral mechanisms because of lower stroke volume. This excess fluid is distributed to dependent areas; in a recumbent position during sleep, fluid gets deposited in the parapharyngeal soft tissue, thereby increasing upper airway resistance and collapsibility, leading to obstructive events.[11]

Observational studies have shown better cardiovascular outcomes in patients with OSA who are compliant with long-term continuous positive airway pressure (CPAP) therapy compared to non-compliant patients with CPAP therapy.[12] In a study by Kaneko et al.,[13] OSA patients on CPAP therapy have been shown

[1–5]Department of Pulmonary, Critical Care and Sleep Medicine, Vardhman Mahavir Medical College & Safdarjung Hospital, New Delhi, India

[6]Department of Endocrinology and Diabetes, Max Super Speciality Hospital, Saket, New Delhi, India

Corresponding Author: Pranav Ish, Department of Pulmonary, Critical Care and Sleep Medicine, Vardhman Mahavir Medical College & Safdarjung Hospital, New Delhi, India, Phone: +91 9958356000, e-mail: pranavish2512@gmail.com

How to cite this article: Mohan S, Ish P, Kumar R, *et al*. Beyond the Breath: Exploring the Complex Nexus of Obstructive Sleep Apnea and Comorbid Conditions. Indian J Sleep Med 2024;19(2):26–30.

Source of support: Nil

Conflict of interest: Dr Rohit Kumar is associated as the National Editorial Board member of this journal and this manuscript was subjected to this journal's standard review procedures, with this peer review handled independently of this editorial board member and his research group.

to improve left ventricular ejection fraction (LVEF) by 9%, decrease in daytime heart rate (HR) and blood pressure (BP), resulting in the more remarkable fall of urinary excretion of epinephrine at night time. However, the SAVE trial, that is, CPAP therapy in non-sleepy patients with OSA, did not show prevention or improvement of cardiovascular comorbidity, which may be due to poor compliance with CPAP in non-sleepy OSA patients.[14] In a study by Bucca et al.,[15] diuretic therapy has resulted in a fall of AHI by 17 in patients with hypertensive diastolic HF due to a reduction in body weight and increased pharyngeal caliber.

Arrhythmias

The most common arrhythmia in OSA is AF. It has been shown in studies and meta-analyses that there is a higher risk of recurrence of AF in patients with OSA as compared to non-OSA patients; CPAP therapy has shown a positive impact in patients with AF secondary to OSA.[16] In a study by Mansukhani et al.,[17] a higher frequency of nocturnal discharge of implantable cardioverter-defibrillator devices (ICD) was seen in OSA compared to non-OSA patients.

Impact on Renal Health

The prevalence study by Hanly.[18] has shown 10 times the risk of OSA in patients with chronic kidney disease (CKD) as compared to the general population. A study by Nicholl et al.[19] reported an increasing prevalence of OSA with worsening eGFR, that is, 27% with eGFR >60, 41% with eGFR < 60 without hemodialysis, and 57% in patients requiring hemodialysis.

The mechanism of OSA in CKD is due to reduced clearance of uremic toxins, hypervolemia, and increased chemoreflex sensitivity.[20]

Chemoreflex response in end-stage renal disease (ESRD) can be enhanced to carbon dioxide (PCO_2) tension due to metabolic acidosis affecting ventilation and apneic threshold; Uremic toxins can lead to myopathy leading to upper airway collapsibility.[20] Fluid redistribution, as in the case of HF to recumbent position, leads to worsening AHI.[11]

A retrospective study by Chu et al.[21] with a sample size of 43,434 individuals from Taiwan has shown an increased risk of CKD in patients with newly diagnosed OSA. CKD in patients with OSA occurs because of stimulation of the sympathetic system and RAAS by apneic episodes causing renal ischemia by systemic and glomerular hypertension, vascular damage, and arterial wall stiffness.[20]

In an observation study by Santos et al.,[22] dialysis is associated with improved uremic clearance and reduced airway congestion, helping in enhancing AHI. Lyons et al.[23] showed a positive correlation between the ultrafiltration amount removed and the AHI reduction. Beecroft et al.[24] showed improvement in polysomnography (PSG) after 3 months of kidney transplant in 18 patients studied.

Continuous positive airway pressure in moderate to severe OSA has a positive impact on kidney filtration.[20] An observational study by Koga et al.[25] has shown that 3 months of CPAP therapy in male patients with renal failure with baseline AHI > 20 can lead to improved eGFR and reduced serum creatinine.

Impact on Neuropsychiatric Health

Stroke

In a meta-analysis published by Li et al.,[26] the incidence of stroke increases in untreated OSA, and data from sleep heart and health studies also suggest the direct relationship of OSA with stroke.[27] Wisconsin study by Artz et al.[28] revealed an increased risk of stroke if AHI > 20.

Autonomic dysfunction and activation of RAAS secondary to high AHI results in changes in cerebral blood flow, which stimulates platelet aggregation, hypercoagulability, and endothelial damage. Untreated OSA also results in accelerated atherosclerosis, impaired glucose tolerance, and cardiac arrhythmia, most commonly AF, which results in a higher risk of stroke.[29]

A meta-analysis by Seiler et al.[30] suggested a high prevalence of OSA after stroke, with one-third having AHI >30. Upper airway muscle function is greatly affected by stroke, resulting in collapsibility. OSA after stroke has poor functional and cognitive outcomes, cerebrovascular morbidity, and more extended hospital stays.[31]

Data from the SAVE trial showed no reduction in the incidence of stroke with CPAP therapy.[14] However, the randomized controlled trial (RCT) by Brill et al.[32] supported short-term as well as long-term functional outcomes and reduced incidence of stroke in patients who are compliant with CPAP therapy. The aim of treatment with CPAP in stroke patients with OSA is to prevent cerebral autoregulation and to protect the ischemic penumbra. Therapy with CPAP improves glycemic control and BP, which further reduces the risk of stroke.

Depression

Depression is a risk factor for the development of OSA later in life. A study by Ohayon MM[33] with 19,000 participants of all ages supported the mutual relationship between OSA and depression. A prospective study from Taiwan by Pan et al.[34] reported that OSA has a high risk of developing depression later in life. An observational study by Jehan et al.[35] reported that 18% of major depressive disorder (MDD) patients fulfill the diagnostic criteria of OSA, and 15% of patients with MDD have increased AHI on PSG.

A meta-analysis done by Povitz et al.[36] reported that CPAP therapy or mandibular advancement device (MAD) in OSA improved depressive symptomatology using depressive scales. CPAP therapy for at least 5 hours for 3 months has been shown to improve depressive symptoms and suicidal ideation. Patients with worse depressive symptoms yielded maximum benefit.[37]

A meta-analysis by AbdelFattah et al.[38] to find anti-depressant efficacy in treating OSA reported that sleepiness is not affected by anti-depressants, and only two anti-depressants had an appositive impact in reducing AHI.

Impact on the Endocrine System

Systemic hypertension, insulin resistance, hyperlipidemia, and central obesity together constitute metabolic syndrome, and its association with OSA has been proven in various studies.[39] Studies have shown a bidirectional relationship between metabolic syndrome and OSA.[40] Metabolic disorders, including hypertension and insulin resistance, are worsened in the presence of OSA.[40]

Obesity

Central obesity leads to fat accumulation in the neck, compromising oropharyngeal diameter. Abdominal traction on the upper airway is also abolished due to abdominal obesity, which increases the risk of upper airway collapsibility.[41]

Epidemiological data confirms a strong association of OSA with obesity; approximately 70% of OSA patients are obese, and 50% of patients with body mass index (BMI) >40 have OSA with AHI >10.[42] OSA patients tend to snack on high-calorie food to boost energy, promoting weight gain, and they have reduced activity.[43]

Weight reduction by exercise or bariatric surgery has proven to reduce OSA.[44] CPAP therapy in OSA has been shown to reduce OSA symptoms, improve mortality, and reduce weight by decreasing insulin resistance.[44]

Diabetes mellitus

European Sleep Apnea Database (ESDA) has shown an independent relationship between type 2 diabetes mellitus, insulin resistance, and OSA. Insulin resistance and diabetes mellitus occur due to intermittent hypoxia and sleep fragmentation, leading to sympathetic stimulation and inflammation.[45] An observational study by Kendzerska et al.[46] which includes 8678 adults has reported that severe OSA (AHI >30) had a 30% increased risk of developing diabetes mellitus as compared to non-OSA patients.

Diabetes mellitus, on the contrary, can cause neuropathy involving upper airway muscles leading to OSA. A prospective study by Huang et al.[47] involving 300,000 subjects concluded OSA to be an independent risk factor for diabetes mellitus.

Data from RCTs on the use of CPAP in diabetic patients with OSA showed varied results; few RCTs have shown insulin sensitivity and reasonable diabetic control, whereas others have reported no benefit.[48] So, the evidence of glycemic control with CPAP therapy is limited.

Hypertension

Landmark studies like Sleep Heart Health study[49] and Wisconsin Cohort study[50] have reported a dose-dependent association of hypertension with OSA. This data has been confirmed by a meta-analysis published by Xia et al.,[51] resulting in no nocturnal dipping of BP and resistance to conventional anti-hypertensives. Possible mechanism of uncontrolled hypertension includes sympathetic excitation and RAAS dysfunction.[52]

Data on hypertension predisposing to OSA is limited. Small studies with limited subjects have shown changes in upper airway tone with fluctuating BP on electromyogram (EMG).[53] A meta-analysis by Khurshid et al.[54] has shown that anti-hypertensives can significantly reduce AHI when used along with diuretics.

Continuous positive airway pressure therapy has been shown to reduce mean BP by 2 mm Hg in 24 hours; the effect is much more significant in patients who have uncontrolled hypertension or a severe degree of desaturation during sleep.[55–56]

Polycystic Ovarian Syndrome (PCOS)

Polycystic ovarian syndrome is a common metabolic disorder in reproductive women and can be associated with infertility, which may further lead to depression. Various metabolic disorders are known to be associated with PCOS, such as obesity, impaired glucose tolerance, type 2 diabetes, dyslipidemia, hypertension, and coronary vessel disease.[57] Meta-analysis published by Helvaci N et al.[57] suggests the overall prevalence of OSA in PCOS is 22%; prevalence was higher at 38% in adults compared to adolescents at 8%.

Polycystic ovarian syndrome has high androgen levels and low estrogen levels and increases visceral fat deposition, leading to upper airway collapsibility.[58] There is limited evidence on OSA leading to PCOS. OSA has been shown to cause insulin resistance and glucose intolerance, which may increase metabolic risk in patients with PCOS.[59]

Continuous positive airway pressure has successfully treated OSA and improved outcomes in PCOS by improving insulin sensitivity, reducing night epinephrine levels, and reducing BP.[60] AutoSet for her (AfH) is a new modality non-inferior to CPAP in young females with PCOS.[60]

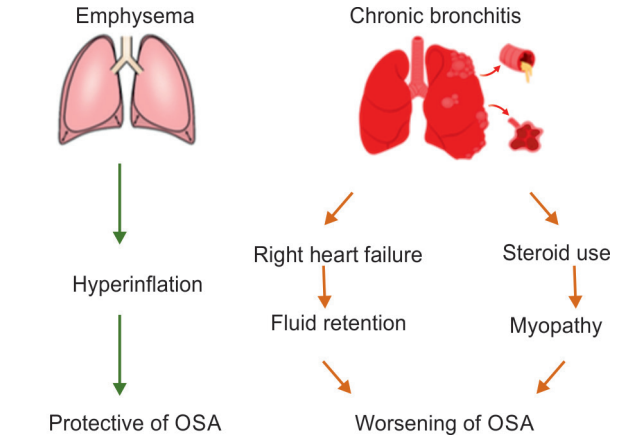

Fig. 1: COPD affecting OSA

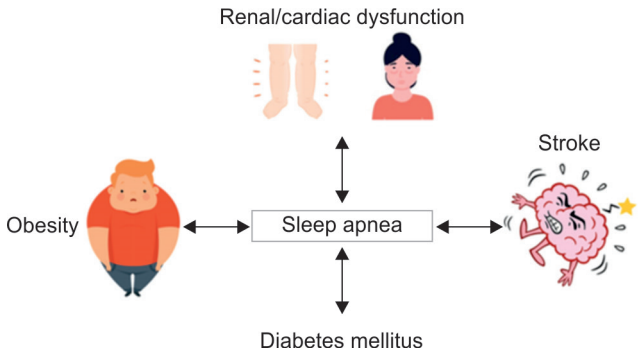

Fig. 2: Bidirectional relationship between comorbidities and OSA

Impact on Other Lung Diseases

Chronic Obstructive Pulmonary Disease (COPD)

The relationship between COPD and OSA is complex; hyperinflation in COPD, as seen in emphysema, is protective for OSA, whereas chronic bronchitis is another phenotype of COPD which has a predisposition to OSA due to a higher incidence of right heart failure leading to fluid retention and myopathy secondary to steroid use promotes OSA (Fig. 1).[61,62]

Data from recent studies suggest an increased incidence of OSA in moderate to severe COPD and more pronounced oxygen desaturation at night if both diseases are present concomitantly.[63]

There is limited data available on OSA predisposing to COPD; an observational study by Greenberg et al.[63] prevalence of COPD and asthma is very high as compared to a matched control population in patients with OSA.

Chronic obstructive pulmonary disease-Obstructive sleep apnea overlap patients should be treated with CPAP; studies have shown increased exacerbations and higher mortality if overlap patients are not treated with CPAP; however, if patients are treated with CPAP, survival seems to be similar to that of COPD or OSA patients (Fig. 2).[64]

Conclusion

Obstructive sleep apnea has shown a bidirectional relationship with various comorbidities. OSA causing various comorbidities is well studied, but the literature on multiple comorbidities causing OSA is minimal. Treating physicians should be aware of the bidirectional relationship between comorbidities and OSA so that it can be detected early and treatment can be offered accordingly.

Orcid

Sanchit Mohan https://orcid.org/0000-0002-3364-1037
Pranav Ish https://orcid.org/0000-0003-1701-4970
Rohit Kumar https://orcid.org/0000-0001-6398-7840
Nitesh Gupta https://orcid.org/0000-0002-5842-5584
Vidushi Rathi https://orcid.org/0000-0002-9735-3915
Nupoor Vaghasia https://orcid.org/0000-0002-1460-2366

References

1. Franklin KA, Lindberg E. Obstructive sleep apnea is a common disorder in the population - a review on the epidemiology of sleep apnea. J Thorac Dis 2015;7(8):1311–1322. DOI: 10.3978/j.issn.2072-1439.2015.06.11.
2. Suri TM, Ghosh T, Mittal S, et al. Systematic review and meta-analysis of the prevalence of obstructive sleep apnea in Indian adults. Sleep Med Rev 2023;71:101829. DOI: 10.1016/j.smrv.2023.101829.
3. McNicholas WT, Bonsignore MR. Sleep apnoea as an independent risk factor for cardiovascular disease: Current evidence, basic mechanisms and research priorities. Eur Respir J 2007;29:156–178. DOI: 10.1183/09031936.00027406.
4. Castro-Grattoni AL, Alvarez-Buvé R, Torres M, et al. Intermittent hypoxia-induced cardiovascular remodeling is reversed by normoxia in a mouse model of sleep apnea. Chest 2016;149:1400–1408. DOI: 10.1016/j.chest.2015.11.010.
5. Jennum P, Tønnesen P, Ibsen R, et al. Obstructive sleep apnea: Effect of comorbidities and positive airway pressure on all-cause mortality. Sleep Med. 2017;36:62–66. DOI: 10.1016/j.sleep.2017.04.018.
6. Yeghiazarians Y, Jneid H, Tietjens JR, et al. Obstructive sleep apnea and cardiovascular disease: A scientific statement from the American Heart Association. Circulation 2021;144:e56–e67. DOI: 10.1161/CIR.0000000000000988.
7. Gottlieb DJ, Yenokyan G, Newman AB, et al. Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure: The sleep heart health study. Circulation 2010;122:352–360. DOI: 10.1161/CIRCULATIONAHA.109.901801.
8. Nicholl DDM, Hanly PJ, Poulin MJ, et al. Evaluation of continuous positive airway pressure therapy on renin–angiotensin system activity in obstructive sleep apnea. Am J Respir Crit Care Med 2014;190:572–580. DOI: 10.1164/rccm.201403-0526OC.
9. Arzt M, Young T, Finn L, et al. Sleepiness and sleep in patients with both systolic heart failure and obstructive sleep apnea. Arch Intern Med 2006;166:1716–1722. DOI: 10.1001/archinte.166.16.1716.
10. Schulz R, Blau A, Börgel J, et al. Sleep apnoea in heart failure. Eur Respir J 2007;29:1201–1205. DOI: 10.1183/09031936.00037106.
11. White LH, Bradley TD. Role of nocturnal rostral fluid shift in the pathogenesis of obstructive and central sleep apnoea. J Physiol 2013;591:Pt 5, 1179–1193. DOI: 10.1113/jphysiol.2012.245159.
12. Doherty LS, Kiely JL, Swan V, et al. Long-term effects of nasal continuous positive airway pressure therapy on cardiovascular outcomes in sleep apnea syndrome. Chest 2005;127:2076–2084. DOI: 10.1378/chest.127.6.2076.
13. Kaneko Y, Floras JS, Usui K, et al. Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N Engl J Med 2003;348:1233–1241. DOI: 10.1056/NEJMoa022479.
14. McEvoy RD, Antic NA, Heeley E, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. N Engl J Med 2016;375:919–931. DOI: 10.1056/NEJMoa1606599.
15. Bucca CB, Brussino L, Battisti A, et al. Diuretics in obstructive sleep apnea with diastolic heart failure. Chest 2007;132:440–446. DOI: 10.1378/chest.07-0311.
16. Congrete S, Bintvihok M, Thongprayoon C, et al. Effect of obstructive sleep apnea and its treatment of atrial fibrillation recurrence after radiofrequency catheter ablation: A meta-analysis. J Evid Based Med 2018;11:145–151. DOI: 10.1111/jebm.12313.
17. Mansukhani MP, Wang S, Somers VK. Sleep, death, and the heart. Am J Physiol Heart Circ Physiol 2015;309(5):H739–49. DOI: 10.1152/ajpheart.00285.2015.
18. Hanly P. Sleep apnea and daytime sleepiness in end-stage renal disease. Semin Dial 2004;17:109–114. DOI: 10.1111/j.0894-0959.2004.17206.x.
19. Nicholl DDM, Ahmed SB, Loewen AHS, et al. Declining kidney function increases the prevalence of sleep apnea and nocturnal hypoxia. Chest 2012;141:1422–1430. DOI: 10.1378/chest.11-1809.
20. Abuyassin B, Sharma K, Ayas NT, et al. Obstructive sleep apnea and kidney disease: A potential bidirectional relationship? J Clin Sleep Med 2015;11:915–924. DOI: 10.5664/jcsm.4946.
21. Chu H, Shih CJ, Ou SM, et al. Association of sleep apnoea with chronic kidney disease in a large cohort from Taiwan. Respirology 2016;21:754–760. DOI: 10.1111/resp.12739.
22. Santos RS, Motwani SS, Elias RM. Chronic kidney disease and sleeping disordered breathing (SDB). Curr Hypertens Rev 2016;12:43–47. DOI: 10.2174/1573402112666160114094222.
23. Lyons OD, Chan CT, Yadollahi A, et al. Effect of ultrafiltration on sleep apnea and sleep structure in patients with end-stage renal disease. Am J Respir Crit Care Med 2015;191:1287–1294. DOI: 10.1164/rccm.201412-2288OC.
24. Beecroft JM, Zaltzman J, Prasad R, et al. Impact of kidney transplantation on sleep apnoea in patients with end-stage renal disease. Nephrol Dial Transplant 2007;22:3028–3033. DOI: 10.1093/ndt/gfm309.
25. Koga S, Ikeda S, Yasunaga T, et al. Effects of nasal continuous positive airway pressure on the glomerular filtration rate in patients with obstructive sleep apnea syndrome. Intern Med 2013;52:345–349. DOI: 10.2169/internalmedicine.52.8468.
26. Li M, Hou WS, Zhang XW, et al. Obstructive sleep apnea and risk of stroke: A meta-analysis of prospective studies. Int J Cardiol 2014;172:466–469. DOI: 10.1016/j.ijcard.2013.12.230.
27. Redline S, Yenokyan G, Gottlieb DJ, et al. Obstructive sleep apnea-hypopnea and incident stroke: The sleep heart health study. Am J Respir Crit Care Med 2010;182:269–277. DOI: 10.1164/rccm.200911-1746OC.
28. Arzt M, Young T, Finn L, et al. Association of sleep-disordered breathing and the occurrence of stroke. Am J Respir Crit Care Med 2005;172:1447–1451. DOI: 10.1164/rccm.200505-702OC.
29. Johnson KG, Johnson DC. Frequency of sleep apnea in stroke and TIA patients: A meta-analysis. J Clin Sleep Med 2010;6:131–137. PMID: 20411688.
30. Seiler A, Camilo M, Korostovtseva L, et al. Prevalence of sleep-disordered breathing after stroke and TIA: A meta-analysis. Neurology 2019;92:e648–e654. DOI: 10.1212/WNL.0000000000006904.
31. Kaneko Y, Hajek VE, Zivanovic V, et al. Relationship of sleep apnea to functional capacity and length of hospitalization following stroke. Sleep 2003;26:293–297. DOI: 10.1093/sleep/26.3.293.
32. Brill AK, Horvath T, Seiler A, et al. CPAP as treatment of sleep apnea after stroke: A meta-analysis of randomized trials. Neurology 2018;90:e1222–e1230. DOI: 10.1212/WNL.0000000000005262.
33. Ohayon MM. The effects of breathing-related sleep disorders on mood disturbances in the general population. J Clin Psychiatry 2003;64:1195–1200, quiz, 1274-6. DOI: 10.4088/jcp.v64n1009.
34. Pan ML, Tsao HM, Hsu CC, et al. Bidirectional association between obstructive sleep apnea and depression: A population-based longitudinal study. Medicine (Baltimore) 2016;95:e4833. DOI: 10.1097/MD.0000000000004833.
35. Jehan S, Auguste E, Pandi-Perumal SR, et al. Depression, obstructive sleep apnea and psychosocial health. Sleep Med Disord 2017;1:000012.
36. Povitz M, Bolo CE, Heitman SJ, et al. Effect of treatment of obstructive sleep apnea on depressive symptoms: Systematic review and meta-analysis. PLoS Med 2014;11:e1001762. DOI: 10.1371/journal.pmed.1001762.
37. Edwards C, Mukherjee S, Simpson L, et al. Depressive symptoms before and after treatment of obstructive sleep apnea in men and

women. J Clin Sleep Med 2015;11:1029–1038. DOI: 10.1007/s11325-019-01954-9.
38. AbdelFattah MR, Jung SW, Greenspan MA, et al. Efficacy of antidepressants in the treatment of obstructive sleep apnea compared to placebo. A systematic review with meta-analyses. Sleep Breath 2020;24:443–453. DOI: 10.1007/s11325-019-01954-9.
39. Drager LF, Togeiro SM, Polotsky VY, et al. Obstructive sleep apnea: A cardiometabolic risk in obesity and the metabolic syndrome. J Am Coll Cardiol 2013;62:569–576. DOI: 10.1016/j.jacc.2013.05.045.
40. Phillips CL, Hoyos CM, Yee BJ, et al. CrossTalk opposing view: Sleep apnoea causes metabolic syndrome. J Physiol 2016;594:4691–4694. DOI: 10.1113/JP272115.
41. Deegan PC, McNicholas WT. Pathophysiology of obstructive sleep apnoea. Eur Respir J 1995;8:1161–1178. DOI: 10.1183/09031936.95.08071161.
42. Resta O, Foschino-Barbaro MP, Legari G, et al. Sleep-related breathing disorders, loud snoring and excessive daytime sleepiness in obese subjects. Int J Obes Relat Metab Disord 2001;25:669–675. DOI: 10.1038/sj.ijo.0801603.
43. Borel AL, Leblanc X, Almeras N, et al. Sleep apnoea attenuates the effects of a lifestyle intervention programme in men with visceral obesity. Thorax 2012;67:735–741. DOI: 10.1136/thoraxjnl-2011-201001.
44. Fritscher LG, Mottin CC, Canani S, et al. Obesity and obstructive sleep apnea-hypopnea syndrome: the impact of bariatric surgery. Obes Surg 2007;17:95–99. DOI: 10.1007/s11695-007-9012-7.
45. Kent BD, Grote L, Bonsignore MR, et al. Sleep apnoea severity independently predicts glycaemic health in nondiabetic subjects: the ESADA study. Eur Respir J 2014;44:130–139. DOI: 10.1183/09031936.00162713.
46. Kendzerska T, Gershon AS, Hawker G, et al. Obstructive sleep apnea and incident diabetes. A historical cohort study. Am J Respir Crit Care Med 2014;190:218–225. DOI: 10.1164/rccm.201312-2209OC.
47. Huang T, Lin BM, Stampfer MJ, et al. A Population-based study of the bidirectional association between obstructive sleep apnea and type 2 diabetes in three prospective U.S. cohorts. Diabetes Care 2018;41:2111–2119. DOI: 10.2337/dc18-0675.
48. Reutrakul S, Mokhlesi B. Obstructive sleep apnea and diabetes: A state of the art review. Chest 2017;152:1070–1086. DOI: 10.1016/j.chest.2017.05.009.
49. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 2000;283:1829–1836. DOI: 10.1001/jama.283.14.1829.
50. Peppard PE, Young T, Palta M, et al. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378–1384. DOI: 10.1056/NEJM200005113421901.
51. Xia W, Huang Y, Peng B, et al. Relationship between obstructive sleep apnoea syndrome and essential hypertension: A dose-response meta-analysis. Sleep Med 2018;47:11–18. DOI: 10.1016/j.sleep.2018.03.016.
52. Crinion SJ, Kleinerova J, Kent B, et al. Non-dipping nocturnal blood pressure correlates with obstructive sleep apnoea severity in normotensive subjects and may reverse with therapy. ERJ Open Res 2021;7:00338-2021. DOI: 10.1183/23120541.00338-2021.
53. Lombardi C, Pengo MF, Parati G. Systemic hypertension in obstructive sleep apnea. J Thorac Dis 2018;10:Suppl. 34, S4231–S4243. DOI: 10.21037/jtd.2018.12.57.
54. Khurshid K, Yabes J, Weiss PM, et al. Effect of antihypertensive medications on the severity of obstructive sleep apnea: A systematic review and meta-analysis. J Clin Sleep Med 2016;12:1143–1151. DOI: 10.5664/jcsm.6054.
55. Tamisier R, Lévy P. Management of hypertension in obstructive sleep apnoea: predicting blood pressure reduction under continuous positive airway pressure. Eur Respir J 2017;50:1701822. DOI: 10.1183/13993003.01822-2017.
56. Pengo MF, Soranna D, Giontella A, et al. Obstructive sleep apnoea treatment and blood pressure: Which phenotypes predict a response? A systematic review and meta-analysis. Eur Respir J 2020;55:1901945. DOI: 10.1183/13993003.01945-2019.
57. Helvaci N, Karabulut E, Demir AU, et al. Polycystic ovary syndrome and the risk of obstructive sleep apnea: A meta-analysis and review of the literature. Endocr Connect. 2017;6(7):437–445.
58. Susan Sam, Esra Tasali. Role of obstructive sleep apnea in metabolic risk in PCOS, Curr Opin Endocr Metab Res 2021:46–51. DOI: 10.1016/j.coemr.2021.01.002.
59. Tasali E, Chapotot F, Leproult R, et al. Treatment of obstructive sleep apnea improves cardiometabolic function in young obese women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2011 Feb;96(2):365–374. DOI: 10.1210/jc.2010-1187.
60. McArdle N, King S, Shepherd K, et al. Study of a Novel APAP algorithm for the treatment of obstructive sleep apnea in Women. Sleep. 2015;38(11):1775–1781. DOI: 10.5665/sleep.5162.
61. Biselli P, Grossman PR, Kirkness JP, et al. The effect of increased lung volume in chronic obstructive pulmonary disease on upper airway obstruction during sleep. J Appl Physiol (1985) 2015;119:266–271. DOI: 10.1152/japplphysiol.00455.2014.
62. Soler X, Gaio E, Powell FL, et al. High prevalence of obstructive sleep apnea in patients with moderate to severe chronic obstructive pulmonary disease. Ann Am Thorac Soc 2015;12:1219–1225. DOI: 10.1513/AnnalsATS.201407-336OC.
63. Greenberg-Dotan S, Reuveni H, Tal A, et al. Increased prevalence of obstructive lung disease in patients with obstructive sleep apnea. Sleep Breath 2014;18:69–75. DOI: 10.1007/s11325-013-0850-3.
64. Machado M-CL, Vollmer WM, Togeiro SM, et al. CPAP and survival in moderate-to-severe obstructive sleep apnoea syndrome and hypoxaemic COPD. Eur Respir J 2010;35:132–137. DOI: 10.1183/09031936.00192008.