Sleep Apnea: Bi-directional Risk with Stroke

Jennifer K. Lynch, MD, FABSM
Medical Director, CoxHealth Stroke Center

Bi-directional

- Sleep apnea <-> Stroke
- Therefore sleep apnea is a risk for stroke and…
- Stroke is a risk factor for sleep apnea and often unmasks it
- Treating sleep apnea before stroke reduces risk and…
- Treating sleep apnea after stroke improves stroke recovery

Sleep apnea definition

- Recurrent pauses in breathing or periods of shallow breathing during sleep.
- 10 seconds or longer per event
- Mild is ≥ 5/hr, able to treat with co-morbidities, moderate ≥15/hr and no additional criteria needed, severe ≥30/hr.
- Apnea is >50% decrease in flow, hypopnea >30% with SaO_2 drop of ≥4%
- May be central (10%), mixed or obstructive (90%)
- Airway remains open in central and blocked in obstructive.

Pickwickian Syndrome

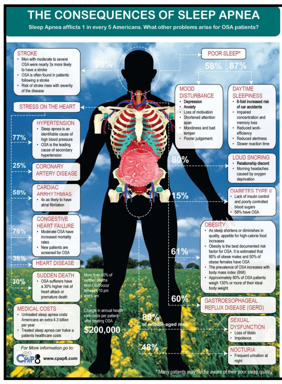
- Joe, the Fat Boy from *The Pickwick Papers* by Charles Dickens in 1836
- Snoring
- Sleepy, even while standing
- Constantly hungry

Not only obesity

- Large tongue
- Small airway behind the tongue
- Large tonsils
- Longer and thicker soft palate
- Low position of the hyoid bone (long necks)
- Brachycephaly (head is wider than it is longer)
- Asians tend to have smaller, more restrictive facial structures

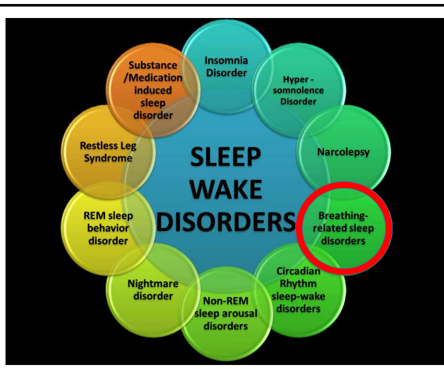
Sleep apnea

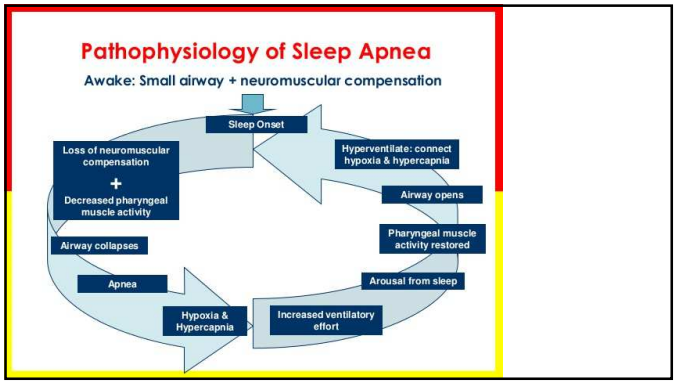
- Common and under-diagnosed.
- May be as high as 20-30% in the middle aged.
- Increases risk by 2-3 times in several prospective studies
- Presence of sleep disordered breathing in stroke patients leads to poor outcomes and increased risk of recurrent stroke
- Associations with:
  - Increased cardiovascular and cerebrovascular disease
  - Atrial fibrillation
  - Obesity and metabolic syndrome
  - Increased dyslipidemia
- Treatment may result in:
  - Improvement in blood glucose levels
  - Inflammation
  - Dyslipidemia

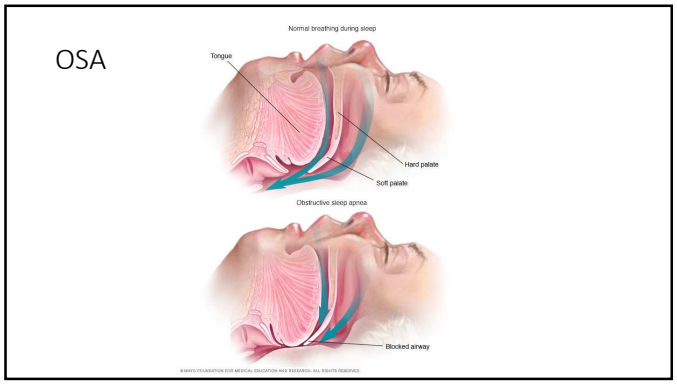

THE CONSEQUENCES OF SLEEP APNEA
Sleep Apnea afflicts 1 in every 5 Americans. What other problems arise for OSA patients?

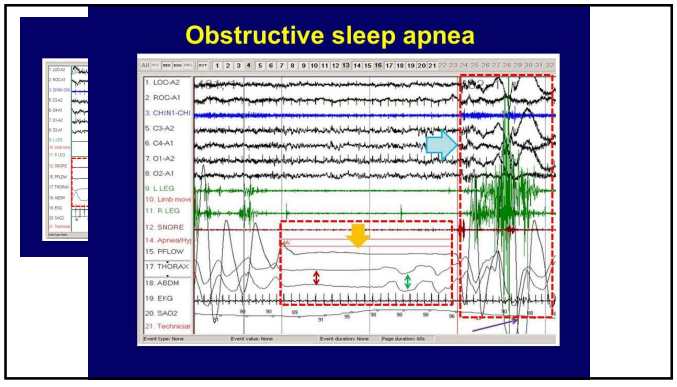

COMPLICATIONS OF SLEEP APNEA:
Sleep Apnea
Hypertension
Obesity
Drowsiness
Fatigue
Diabetes
Motor Vehicular Accident
Job Impairment
Arrythmia
Heart Attack
Headache
Stroke
Lung Hypertension
Dementia & Memory Loss
Impotence


SLEEP WAKE DISORDERS
Insomnia Disorder
Hyper - somnolence Disorder
Narcolepsy
Breathing-related sleep disorders
Circadian Rhythm sleep-wake disorders
Non-REM sleep arousal disorders
Nightmare disorder
REM sleep behavior disorder
Restless Leg Syndrome
Substance /Medication induced sleep disorder

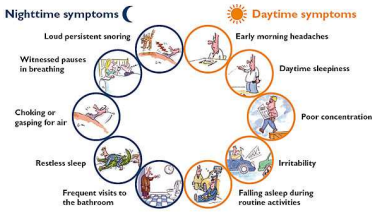

SLEEP WAKE DISORDERS
Insomnia Disorder
Hyper - somnolence Disorder
Narcolepsy
Breathing-related sleep disorders
Circadian Rhythm sleep-wake disorders
Non-REM sleep arousal disorders
Nightmare disorder
REM sleep behavior disorder
Restless Leg Syndrome
Substance /Medication induced sleep disorder


Pathophysiology of Sleep Apnea
Awake: Small airway + neuromuscular compensation
Sleep Onset
Loss of neuromuscular compensation
+
Decreased pharyngeal muscle activity
Airway collapses
Apnea
Hypoxia & Hypercapnia
Increased ventilatory effort
Arousal from sleep
Pharyngeal muscle activity restored
Airway opens
Hyperventilate: connect hypoxia & hypercapnia


OSA
Normal breathing during sleep
Tongue
Hard palate
Soft palate
Obstructive sleep apnea
Blocked airway


Obstructive sleep apnea
1. LOC-A2
2. ROC-A1
3. CHIN1-CHI
5. C3-A2
6. C4-A1
7. O1-A2
8. O2-A1
9. L LEG
10. Limb move
11. R LEG
12. SNORE
14. Apnea/Hyp
15. PFLOW
17. THORAX
18. ABDM
19. EKG
20. SaO2
21. Technician

Many symptom consequences of sleep apnea

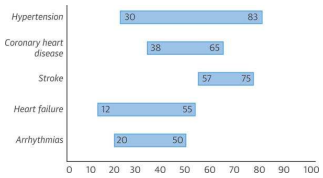


Obstructive sleep apnea

- Prevalence may be as high as 20-30% in middle-aged (34% of men and 17% of women and largely undiagnosed
- Increasingly linked to cardiovascular and cerebrovascular disease
- Associated with obesity and metabolic syndrome, most likely from reduced androgens
- Increased dyslipidemia associated with untreated OSA
- Treatment can result in improvement in lipid levels
- This may result in improvement in multiple areas: Blood glucose levels, inflammation and dyslipidemia

Before the Stroke…

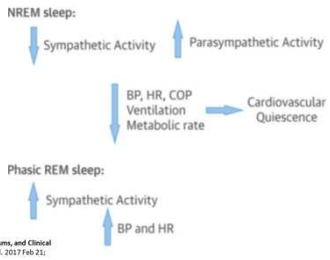
Medical Consequences of Sleep Apnea



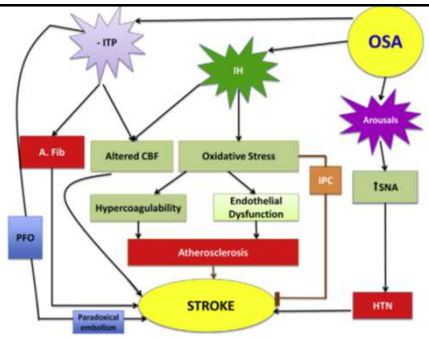
Prevalence (%) of OSA in CVD

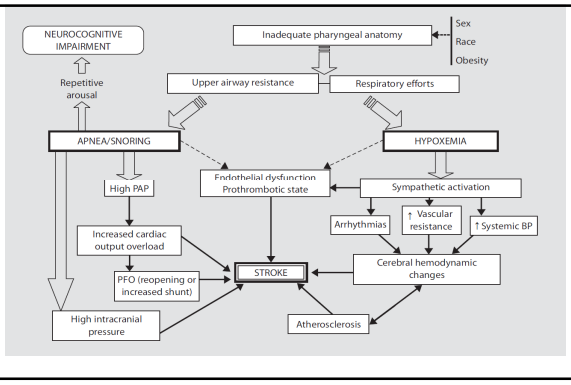
Javaheri S, et al. **Sleep Apnea: Types, Mechanisms, and Clinical Cardiovascular Consequences.** J Am Coll Cardiol. 2017 Feb 21; 69(7): 841–858.

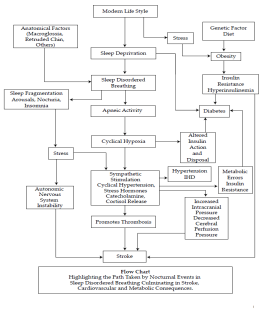
Normal Cardiovascular Changes in NREM and REM Sleep



Javaheri S, et al. **Sleep Apnea: Types, Mechanisms, and Clinical Cardiovascular Consequences.** J Am Coll Cardiol. 2017 Feb 21; 69(7): 841–858.



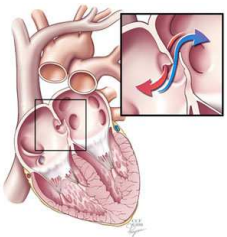




Iyer SR & Iyer RR. **Sleep, Ageing and Stroke- Newer Directions in Management of Stroke. J Assoc Physicians India.** 2010 Jul;58:442-6.

Sleep Apnea and Patent Foramen Ovale

- Prevalence of PFO in sleep apnea significantly higher (69 vs 17%)
  - Possibly due to transient infrequent elevation of right-sided pressure during apnea and subsequent opening of PFO
  - Possible right left shunt as well as increased blood this causes to be in sleep apnea may raise the likelihood of embolism



Atrial fibrillation recurrence after cardioversion

- Recurrence 82% in non-compliant or untreated vs. 42% in treated OSA (P= 0.009)
- Worse sleep apnea predicted recurrence in untreated OSA.
  - SaO_2 drop 8% vs 18% (P=0.034)
  - 4% vs 23% of night with SaO_2 <90% (P=0.063)

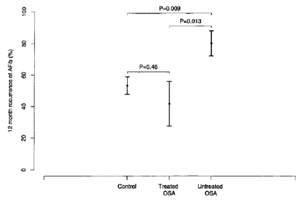
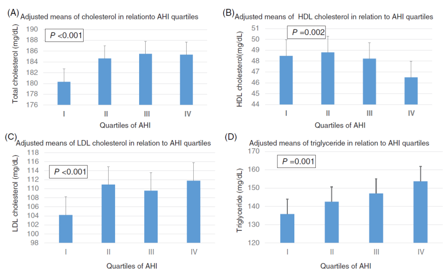


Figure 1. Recurrence of AF at 12 months comparing patients who did not have sleep studies (controls) with treated OSA patients and with untreated (including noncompliant) OSA patients (mean±SD).

Kanagala R, Murali N, Frideman P, et al: Obstructive sleep apnea and the recurrence of atrial fibrillation. Circulation 2003; 107: 2589–2594.

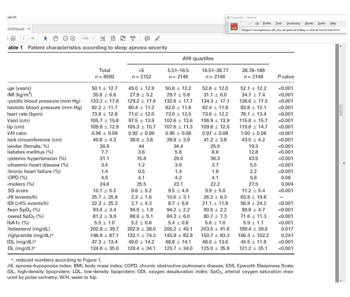
OSA and Dyslipidemia



Gündüz C, Basoglu OK et al. Obstructive sleep apnoea independently predicts lipid levels. Data from the European Sleep Apnea Database. Respirology 2018 doi:10.1111/resp.13372

Patient Characteristics According to Sleep Apnea Severity

Gündüz C, Basoglu OK et al. Obstructive sleep apnoea independently predicts lipid levels. Data from the European Sleep Apnea Database. Respirology 2018 doi:10.1111/resp.13372

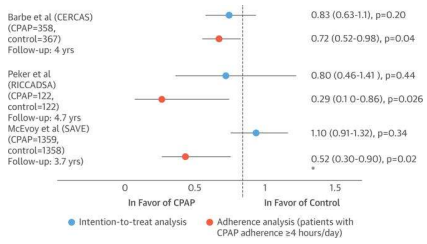


able 1 Patient characteristics according to sleep apnoea severity

		AHI quartiles				
	Total n = 8592	<5 n = 2152	5.51–16.5 n = 2146	16.51–38.77 n = 2146	38.78–188 n = 2148	P-value
ge (years)	50.1 ± 12.7	45.0 ± 12.9	50.6 ± 12.2	52.6 ± 12.0	52.1 ± 12.2	<0.001
MI (kg/m^2)	30.8 ± 6.6	27.9 ± 5.2	29.7 ± 5.8	31.1 ± 6.0	34.7 ± 7.4	<0.001
ystolic blood pressure (mm Hg)	133.2 ± 17.6	129.2 ± 17.4	132.6 ± 17.7	134.3 ± 17.1	136.6 ± 17.3	<0.001
iastolic blood pressure (mm Hg)	82.2 ± 11.7	80.4 ± 11.2	82.0 ± 11.6	82.4 ± 11.8	83.8 ± 12.1	<0.001
eart rate (bpm)	73.9 ± 12.8	71.0 ± 12.0	73.0 ± 12.5	73.6 ± 12.2	78.1 ± 13.4	<0.001
Vaist (cm)	105.7 ± 15.8	97.5 ± 13.9	102.6 ± 13.6	106.9 ± 13.9	115.8 ± 15.7	<0.001
lip (cm)	109.6 ± 12.9	105.3 ± 10.7	107.6 ± 11.3	109.8 ± 12.0	115.6 ± 14.7	<0.001
V/H ratio	0.96 ± 0.09	0.92 ± 0.09	0.95 ± 0.08	0.97 ± 0.08	1.00 ± 0.08	<0.001
leck circumference (cm)	40.8 ± 4.3	38.6 ± 3.8	39.9 ± 3.9	41.2 ± 3.8	43.5 ± 4.2	<0.001
ender (female, %)	30.9	44	34.4	25.9	19.3	<0.001
iabetes mellitus (%)	7.7	3.6	5.8	8.6	12.8	<0.001
ystemic hypertension (%)	31.1	15.8	29.0	36.3	43.5	<0.001
schaemic heart disease (%)	3.4	1.2	3.0	3.7	5.5	<0.001
hronic heart failure (%)	1.4	0.5	1.4	1.6	2.2	<0.001
OPD (%)	4.5	4.1	4.2	4.1	5.6	0.06
mokers (%)	24.6	25.5	23.1	22.2	27.5	0.004
SS score	10.1 ± 5.2	9.6 ± 5.2	9.5 ± 4.9	9.9 ± 5.0	11.2 ± 5.4	<0.001
HI (events/h)	25.7 ± 25.9	2.3 ± 1.6	10.6 ± 3.1	26.2 ± 6.3	63.9 ± 19.8	—
DI (≥4% events/h)	22.3 ± 25.3	2.7 ± 4.3	8.7 ± 6.6	21.1 ± 11.8	56.9 ± 24.2	<0.001
lean SpO_2 (%)	93.4 ± 3.4	94.9 ± 1.8	94.2 ± 2.2	93.6 ± 2.2	90.8 ± 4.7	<0.001
owest SpO_2 (%)	81.2 ± 9.9	88.0 ± 5.1	84.3 ± 6.0	80.7 ± 7.3	71.6 ± 11.3	<0.001
lbA1c (%)	5.5 ± 1.0	5.2 ± 0.8	5.4 ± 0.8	5.6 ± 1.0	5.9 ± 1.1	<0.001
holesterol (mg/dL)	202.8 ± 39.7	202.9 ± 38.0	205.2 ± 40.1	203.5 ± 41.6	199.4 ± 39.0	0.017
riglyceride (mg/dL)*	148.8 ± 87.1	132.1 ± 74.3	145.9 ± 82.9	150.7 ± 83.3	166.3 ± 102.2	0.241
IDL (mg/dL)*	47.3 ± 13.4	49.0 ± 14.2	48.8 ± 14.1	48.0 ± 13.6	44.5 ± 11.8	<0.001
DL (mg/dL)*	124.6 ± 35.0	128.4 ± 34.1	125.7 ± 34.0	125.0 ± 35.9	121.2 ± 35.1	<0.001

*, reduced numbers according to Figure 1.
HI, apnoea–hypopnoea index; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ESS, Epworth Sleepiness Scale; IDL, high-density lipoprotein; LDL, low-density lipoprotein; ODI, oxygen desaturation index; SpO_2, arterial oxygen saturation meaured by pulse oximetry; W/H, waist to hip.

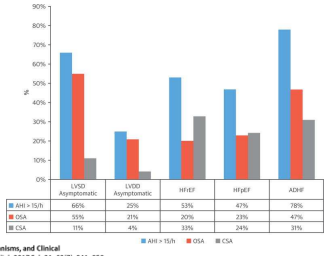
Effect of CPAP Treatment on CV Risk



Javaheri S, et al. **Sleep Apnea: Types, Mechanisms, and Clinical Cardiovascular Consequences.** J Am Coll Cardiol. 2017 Feb 21; 69(7): 841–858.

*In the McEvoy study, the significant CV improvement in patients who used CPAP ≥4 h/day was only achieved in the risk of a cerebrovascular event, but not in cardiovascular outcome

Sleep Apnea is Prevalent in Left Ventricular Dysfunction

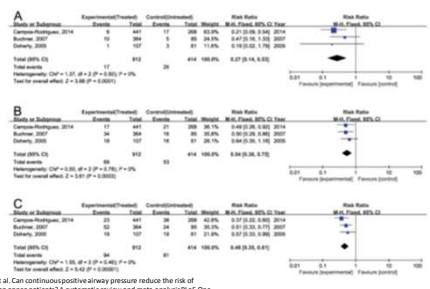


	LVSD Asymptomatic	LVDD Asymptomatic	HFrEF	HFpEF	ADHF
AHI > 15/h	66%	25%	53%	47%	78%
OSA	55%	21%	20%	23%	47%
CSA	11%	4%	33%	24%	31%

Javaheri S, et al. **Sleep Apnea: Types, Mechanisms, and Clinical Cardiovascular Consequences.** J Am Coll Cardiol. 2017 Feb 21; 69(7): 841–858.

CPAP Treatment Reduces Incidence of CV events

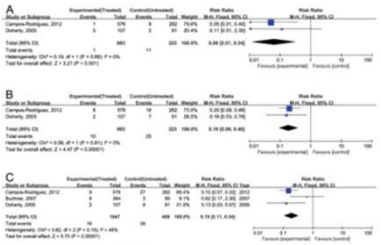
(A) Incidence of stroke. (B) Incidence of cardiac disease. (C) Incidence of overall CVE.



Kim Y, Koo YS, Lee HY, et al. Can continuous positive airway pressure reduce the risk of stroke in obstructive sleep apnea patients? A systematic review and meta-analysis PLoS One. 2016; 11(1):e0146317.

CPAP Treatment Reduces Mortality of CV Events

(A) Mortality from stroke. (B) Mortality from cardiac disease. (C) Mortality from overall CVE



Kim Y, Koo YS, Lee HY, et al. Can continuous positive airway pressure reduce the risk of stroke in obstructive sleep apnea patients? A systematic review and meta-analysis PLoS One. 2016; 11(1):e0146317.

And don't forget this one! As if the others weren't enough

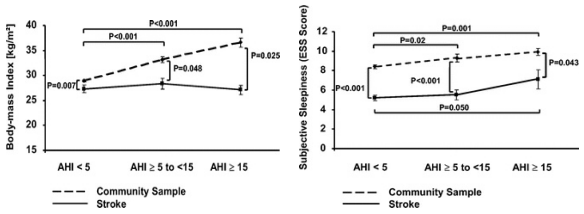
- Erectile dysfunction seen in 69% with OSA vs. 34% without OSA ($p<0.001$)
- OR was 0.45 to have ED in absence of OSA.
- Correlates with mean nocturnal SaO_2 so intermittent hypoxemia may be specific contributor.
- Treatment with CPAP improved ratings of erectile function and sexual satisfaction

Budweiser S, Enderlein, S Jörres RA, Hitzl AP, Wieland WF, Pfeifer M, Arzt M. Sleep apnea is an independent correlate of erectile and sexual dysfunction. J Sex Med 2009 Nov;6(11):3147-57

Pascual M et al. Erectile dysfunction in obstructive sleep apnea patients. A randomized treat on the effects of CPAP. PLoS One. 2018 Aug 8;13(8)

After the Stroke… or CPAP

What's unique about OSA after stroke?



Sleepiness, snoring and obesity are less prevalent in stroke patients

Relationship between BMI and OSA severity less apparent after stroke!

BMI ≥ 30 and OSA: Non-stroke population: OR 4.7(3.4-6.2) vs Stroke population: OR 1.1 (0.4-2.9)

Arzt M, Young T et al. Dissociation of Obstructive Sleep Apnea From Hypersomnolence and Obesity in Patients With Stroke. Stroke 2010 41(3) e129-134.

How common is it?

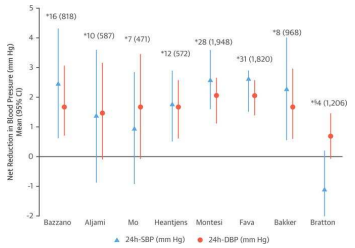
Table 3—Percentage of stroke or TIA patients with SDB stratified by AHI

Cutpoint	# Studies (# patients)	% (95% CI)
AHI > 5	9 (908)	72 (60–81)
AHI > 10	24 (1980)	63 (58–68)
AHI > 20	15 (1405)	38 (31–46)
AHI > 30	10 (865)	29 (21–37)
AHI > 40	3 (318)	14 (7–25)
Central*	17 (1286)	7 (5–12)

*Percentage of patients who had primarily central apnea

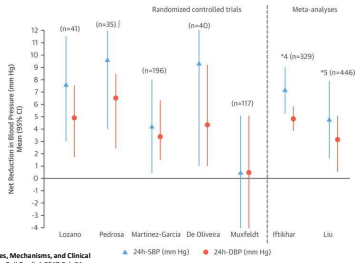
Johnson KG & Johnson DC. Frequency of sleep apnea in stroke and TIA patients: a meta-analysis. *J Clin Sleep Med* 2010;6(2):131-137.

Effect of CPAP Therapy on BP in Patients With Hypertension



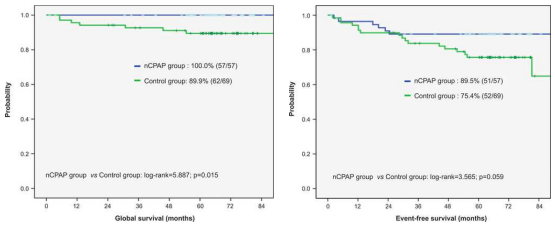
Javaheri S, et al. **Sleep Apnea: Types, Mechanisms, and Clinical Cardiovascular Consequences.** J Am Coll Cardiol. 2017 Feb 21; 69(7): 841–858.

Effect of CPAP Therapy on BP in Patients With Resistant Hypertension



Javaheri S, et al. **Sleep Apnea: Types, Mechanisms, and Clinical Cardiovascular Consequences.** J Am Coll Cardiol. 2017 Feb 21; 69(7): 841–858.

Cardiovascular Survival after Stroke



Parra O, Sánchez-Armengol Á, Capote F, et al. Efficacy of continuous positive airway pressure treatment on 5-year survival in patients with ischaemic stroke and obstructive sleep apnea: a randomized controlled trial. J Sleep Res. 2015; 24:47–53.

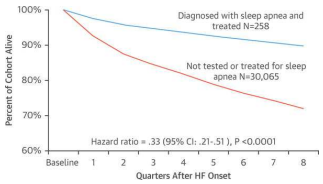
Cardiovascular Events and Mortality

5-year follow-up

	nCPAP group (*n* = 57)	Control group (*n* = 69)
Cardiovascular events		
Stroke	3	8
Transient ischaemic attack	1	1
Angina	1	1
Myocardial infarction	1	0
Other events	0	0
Deaths	6	9
Cardiovascular-related deaths	0	7
Non-cardiovascular-related deaths	6	2

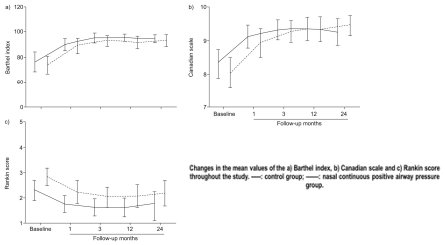
Parra O, Sánchez-Armengol Á, Capote F, et al. Efficacy of continuous positive airway pressure treatment on 5-year survival in patients with ischaemic stroke and obstructive sleep apnea: a randomized controlled trial. J Sleep Res. 2015; 24:47–53.

Comparative Survival of HF Patients Treated for and Not Tested for Sleep Apnea



Javaheri S, et al. **Sleep Apnea: Types, Mechanisms, and Clinical Cardiovascular Consequences.** J Am Coll Cardiol. 2017 Feb 21; 69(7): 841–858.

Stroke outcomes if treated with CPAP



Changes in the mean values of the a) Barthel index, b) Canadian scale and c) Rankin score throughout the study. —: control group; ——: nasal continuous positive airway pressure group.

Parra, O., Sanchez-Armengol, A., Bonnin, M. et al. Early treatment of obstructive apnea and stroke outcome: a randomised controlled trial. Eur. Respir. J., 2011, 37: 1128–1136.

Early Improvement in Stroke Recovery with CPAP

TABLE 2 Percentage of patients with improvement in neurological parameters 1 month after stroke

	nCPAP group	Control group	OR (95% CI)	p-value#
Subjects n	57	69		
Barthel index, improvement ⩾1 point of disability				
All patients	43/52 (82.7)	45/54 (83.3)		0.567
Excluding patients with less severe stroke	26/35 (74.3)	30/39 (76.9)		0.502
Rankin scale, reduction ⩾1 point per category				
All patients	30/33 (90.9)	18/32 (56.3)	7.78 (1.73–39.84)	0.002
Excluding patients with less severe stroke	21/24 (87.5)	14/28 (50.0)	7.00 (1.47–37.86)	0.004
Canadian scale, increase of ⩾0.5 points				
All patients	45/51 (88.2)	40/55 (72.7)	2.81 (0.91–9.07	0.038
Excluding patients with less severe stroke	33/39 (84.6)	28/43 (65.1)	2.95 (0.91–9.93)	0.038

Data are presented as n/N (%), unless otherwise stated. nCPAP: nasal continuous positive airway pressure. #: between the nCPAP group and the control group (Chi-squared test).

Parra, O., Sanchez-Armengol, A., Bonnin, M. et al. Early treatment of obstructive apnea and stroke outcome: a randomised controlled trial. Eur. Respir. J., 2011, 37: 1128–1136.

Lipid metabolism and OSA/CPAP

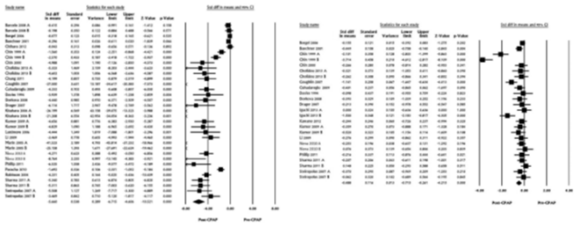
Chronic intermittent hypoxia (reversed by CPAP):
- Upregulates lipoprotein secretion
- ↑ free fatty acid flux to the liver
- Induces sympathetic activity which may induce lipolysis

Insulin resistance (improved with CPAP):
- ↑ total cholesterol and LDL by ↓ LDL receptors and ↓ LDL catabolism
- ↓ inflammatory markers

Hypersomnia improvements with increased activity

Hypersomnia with effects on leptins and ghrelins

Total cholesterol and LDL pre- and post-Tx



Nadeem R, Singh M, Nida M, Kwon S, Sajid H, Witkowski J, Pahomov E, Shah K, Park W, Champeau D. Effect of CPAP treatment for obstructive sleep apnea hypopnea syndrome on lipid profile: a meta-regression analysis. *J Clin Sleep Med* 2014;10(12):1295-1302.

Stroke Recurrence (25% of total stroke) and OSA

A	Odd's Ratio	95 % Confidence Interval	p-level
RDI ≥ 10/h	3.50	1.10–11.20	< 0.05
Gender	1.80	0.59–5.52	n. s.
Age	1.02	0.97–1.07	n. s.
Cumul. RF	0.66	0.34–1.28	n. s.
Diabetes	4.50	1.20–16.3	< 0.05
B	**Odd's Ratio**	**95 % Confidence Interval**	**p-level**
RDI ≥ 50/h	9.70	1.60–58.34	< 0.05
Gender	1.70	0.59–5.38	n. s.
Age	1.02	0.97–1.06	n. s.
Cumul. RF	0.73	0.37–1.40	n. s.
Diabetes	4.10	1.14–14.60	< 0.05

	First Stroke N = 77	Second Stroke N = 25	
Age (years)	63.1 (13.6)	69.0 (13.4)	n. s.
Women (n)	28 (36)	6 (24)	n. s.
BMI (kg/m²)	26.3 (4.5)	26.1 (3.9)	n. s.
Neck circ. (cm)	42.5 (4.9)	42.5 (3.5)	n. s.
Cumul. RF (n)	2.0 (0.8)	2.2 (1.0)	n. s.
Hypertension (%)	55 (71)	20 (80)	n. s.
Hypercholest. (%)	51 (66)	15 (60)	n. s.
Nicotine (%)	32 (42)	8 (32)	n. s.
Diabetes (%)	13 (17)	11 (44)	p < 0.05
NIH-SS (pt)	7.1 (6.2)	5.3 (4.2)	n. s.
RDI (events/h)	15.1 (14.9)	26.6 (20.7)	p < 0.05
RDI ≥ 10/h (%)	40 (52)	20 (80)	p < 0.05
RDI ≥ 50/h (%)	2 (3)	5 (20)	p < 0.05
Stroke etiology			
Large Artery atheroscl.	22 (29)	7 (28)	n. s.
Cardial embolism	30 (39)	8 (32)	n. s.
Lacunar stroke	15 (20)	5 (20)	n. s.
Arterial dissection	5 (6)	1 (4)	n. s.
undetermined	5 (6)	4 (16)	n. s.

Birkbak J; Clark AJ; Rod NH. The effect of sleep disordered breathing on the outcome of stroke and transient ischemic attack: a systematic review. *J Clin Sleep Med* 2014;10(1):103-108.

Sleep apnea screening uncommon after stroke

- Non-academic stroke center
- Only 17% of patients reported being offered sleep apnea testing pre-stroke.
- After stroke: 5% report being questioned about snoring, 9% about sleepiness, 6% offered sleep studies.
- But likelihood is 72% (AHI >5)

Brown DL, Jiang X, Li C, et al. Sleep apnea screening is uncommon after stroke. *Sleep Med* 2018 S 1389-9457 (18).

All it takes is a pulse oximetry (to screen)

- Of 115 stroke patients, 75 with oxygen desaturation index >4% of >10/hr, mean was 29 ± 30.
- Association with atrial fibrillation and ⬆ODI (P=0/005)
- Association between discharge disposition rehab vs. home and ⬆ODI (P=0.005, OR 3.76)

Yaddanpudi SS, Pineda MC et al. High-Resolution Pulse Oximetry (HRPO): A Cost-Effective Tool in Screening for Obstructive Sleep Apnea (OSA) in Acute Stroke and Predicting Outcome. J Stroke Cerebrovasc Dis. 2018 Nov;27(11):2986-2992.

Summary

- Sleep apnea is a risk for stroke and many conditions that predispose to stroke
- Treatment of sleep apnea can reduce the risk of new or recurrent stroke when present
- Treatment of sleep apnea can lead to improved stroke outcomes
- Current screening is inadequate

Thanks! Your lecture cured my sleep disorder.

Excessive sleepiness in OSA: OSA is associated with structural changes in gray and white matter that are been linked to reduced neurocognitive performance and compromised neurocognitive activity in patients with OSA

Oxidative injury
In an animal model of severe sleep apnea, chronic intermittent hypoxia showed significant oxidative injury to certain wake-promoting dopaminergic and noradrenergic neurons, compared with sham controls. This resulted in a 40% loss of dopaminergic and noradrenergic neurons at 6 months.[7,12]

Degeneration of wake-promoting neurons
Chronic fragmented sleep caused a significant loss of 50% ($P<0.001$) of noradrenergic neurons and 25% loss of orexigenic neurons involved in wake promotion in an animal model, which persisted after 4 weeks of recovery sleep.[9]

Reduced gray matter
As compared to healthy controls, studies have indicated that untreated OSA is associated with reduced gray matter volume in brain regions, including those involved in wakefulness and neurocognitive performance.[9,10]

Structural changes to white matter
In patients adherent to CPAP (≥6 hours), ES was associated with structural changes to white matter, potentially indicating compromised neuroconnectivity. Some structural changes correlated with clinical measures of ES.[11]

And a bit on stroke during sleep…

- Now you may have the luxury of tPA or IR if you wake with a stroke.
- EXTEND allows for tPA up to 9 hours from onset using RAPID software in non-LVO stroke.
- WAKE-UP

- G€£¥©®™±≠≤≥÷×∞μαβ←↑→↓↔↗↘⬆⬇
- Üä
- Ääë
- Üü
- Gündüz C, Basoglu OK et al. Obstructive sleep apnoea independently predicts lipid levels. Data from the European Sleep Apnea Database. Respirology 2018 doi:10.1111/resp.13372
- Z, C
- ö