



SLEEP & STROKE

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Circadian Variations Influential in Circulatory & Vascular Phenomena

- Endocrine secretions
- Thermo regulations
- Renal Functions
- Respiratory control
- Heart Rhythm
- Hematologic parameters
- Immune system
- Drug metabolism

- ↑ Plasma catecholamines- 6.00 am - noon
- ↓ Fibrinolytic activity
- ↑ Platelet aggregability
- ↑ Stroke occurrence

Overview

- Sleep apnea (OSA)
- Stroke
- How OSA/Stroke are connected
- Supporting Evidence
- Prevention/therapy
- Summary

Sleep Apnea

- 18 million affect (1 in 15 Americans)
Prevalence (Men 24%, Women 9%)
- 10 - 20% are children
- Untreated or undiagnosed >80%
- Health cost for individual with untreated sleep apnea is about \$1,336/yr

National Sleep Foundation

Who snores more, Men or women?



SNORING

- Habitual Snoring
- SDB

Snoring

- Studies suggest it is a risk factor for ischemic stroke
- Multiple Studies show it increases blood pressure
- Vibration from snoring increase plaque formation in the carotid artery.

SDB & STROKE

- Abundant circumstantial evidence points to a causal association between SDB & stroke

Snoring

- Study from Japan
- 167 patients with OSA
- mean age - 47
- After control for High BP, DM, high cholesterol
- Results shows patients with
 - High AHI have increase carotid artery thickness (measured by ultrasound)
 - Decrease thickness after CPAP therapy

Suzuki et al, Sleep, 2004

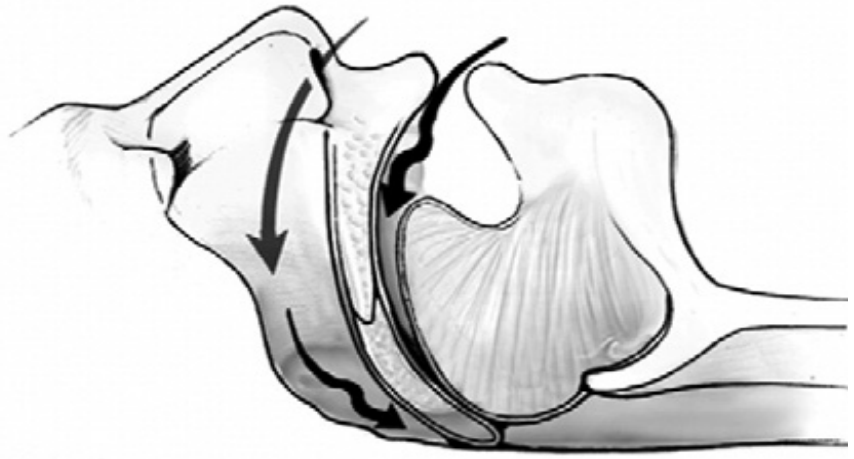
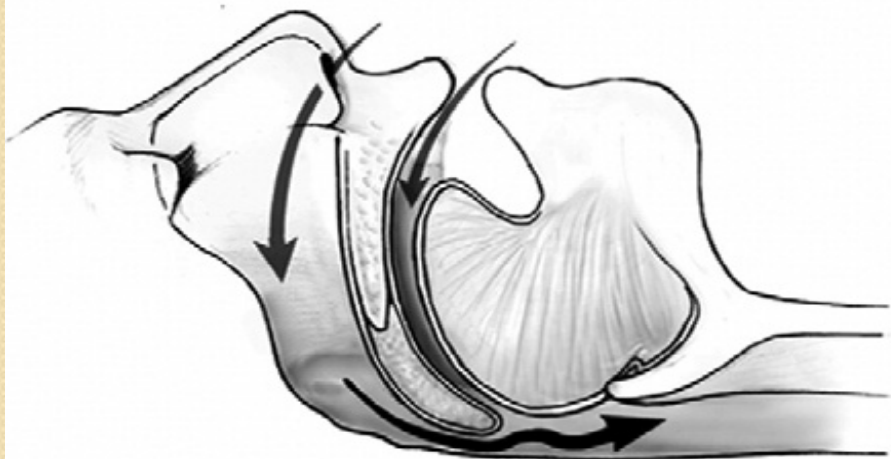
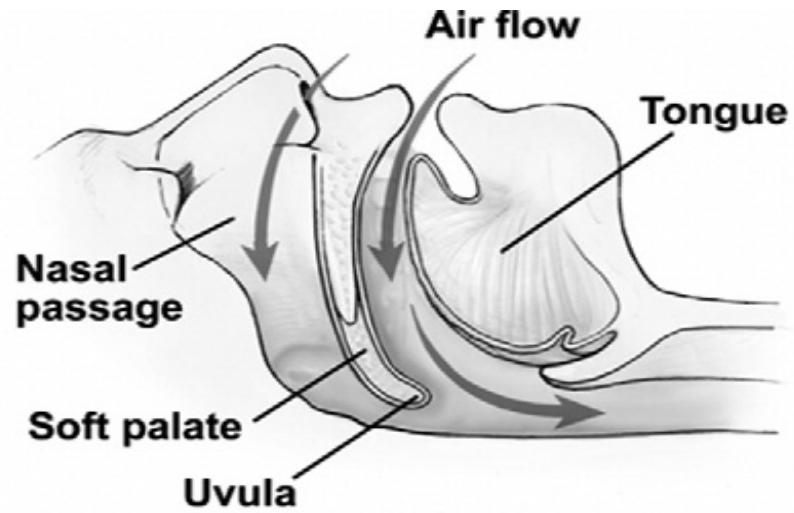
Types of Sleep Apnea

- **Obstructive** (Apnea and Hypopnea)
- Central Sleep Apnea
- Mixed Sleep Apnea

What is Obstructive sleep apnea

- Recurrent episode of airway obstruction during sleep
- Lasting at least 10 seconds
- Can be associated with arousal or decrease in oxygen level

OSA



EPIDEMIOLOGY OF OSA

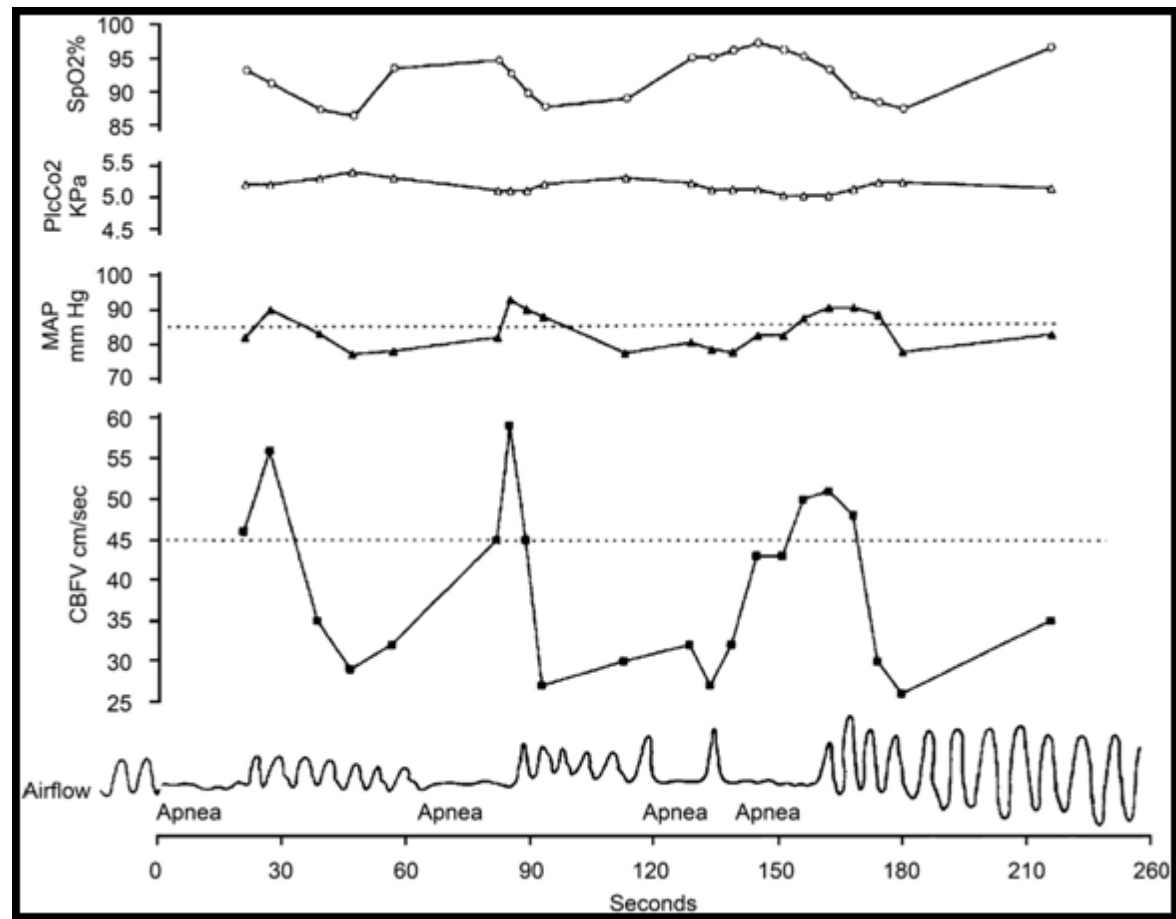
- 20% of general population
- Obesity & age - ↑ risk
- AHI
- > 5 events/ hr with EDS, snoring > 15 events/ hr
- Sleep apnea in stroke : 50 % -70%
- Most common SDB in stroke → OSA

How is OSA measured

AHI (Apnea/hypopnea index) or
RDI (Respiratory Disturbance Index)

- AHI < 5 (normal)
- AHI 5 -15 (mild)
- AHI >15 - 30 (moderate)
- AHI > 30 (severe)

PHYSIOLOGIC RECORDINGS IN A PATIENT WITH OBSTRUCTIVE SLEEP APNEA



Symptoms/signs of OSA

- Snoring
- Gasping or choking from sleep
- Excessive daytime sleepiness
- Daytime fatigue
- Cognitive dysfunction (memory, concentration)
- Change in mood (irritable)
- Unrefreshed sleep

Untreated OSA increases your Risk

- High blood pressure
- Heart disease (abnormal heart rhythm, heart failure)
- **Stroke**
- Depression
- Diabetes
- Accidents
- Death

OSA & STROKE

Shared Risk Factors

- Hypertension
- Insulin resistance
- CAD
- Heart failure
- Arrhythmias AF

Brain scan in OSA patients

- Brain MRI shows silent brain infarcts in 25% of patient with moderate to severe OSA

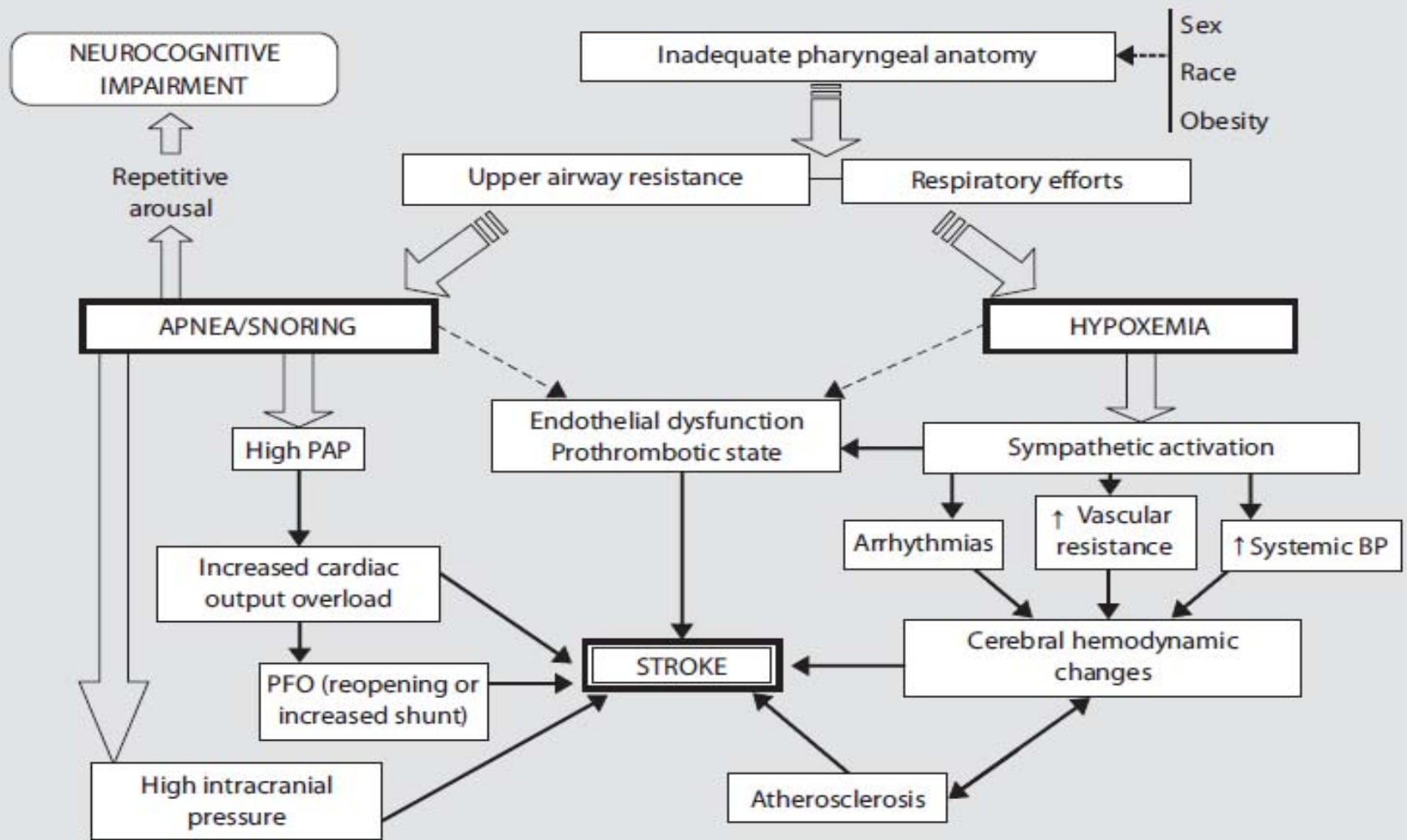
Minoguchi et al, AM J Respir Crit care Med, 2007

- Higher prevalence of sleep apnea in patients with vascular dementia compared with patients with Alzheimer's disease or control of similar age

Erkinjuntti et al, sleep, 1987

INDEPENDENT RISK FACTORS

- Sympathetic activation → tachyarrhythmias
- Blood pressure fluctuation → impaired cerebral hemodynamics
- Hypoxemia associated enhanced inflammation & oxidative stress
- Systemic inflammation due to activated nuclear factors kappa-B mediated inflammatory pathways
- Promotion of atherosclerosis & thrombosis
- Abnormal coagulation markers
- ↑ Increased plasma fibrinogen levels
- ↑ Platelet reactivity
- R → L shunting through PFO



HYPERTENSION & OSA

- Autonomic & hemodynamic responses of OSA → surges in HR & BP
- Sleep Heart Health Study →
RR of HTn in severe OSA vs none was 1.37 (95% CI 1.03-1.83)
- Wisconsin sleep cohort study ↑ risk of HTN after adjustment
- Treatment with CPAP ↓ HTN

? MECHANISMS

- Patients with OSA → ↑ sympathetic activity
- Augmentation of RAS in face of chronic OSA – induces hypoxia
- Risk for medically refractory HTN

APNEA- RESPONSES

- Cardiac → ↓ stroke volume
↓ HR
↓ cardiac output
- Progressive oxyhemoglobin desaturation
- Gradual hypercapnia
- Cardiac arrhythmias → ↓ O₂ sat <65%

REM SLEEP- MOST VULNERABLE!

- REM sleep related atonia of dilator oropharyngeal muscles
- loss of respirator drive dependency on chemoreceptor reflex activity
- Prolonged episode of OSA
- Profound hypoxemia → cardiac rhythm changes
- ↑ cardiovascular & cerebrovascular risk

OSA & STROKE

- ? TIA & silent infarcts in night.
- MCA flow during apnea.

Study

- Conducted at Yale Medical Center
- 1022 participants enrolled but only 842 completed
 - 573 with OSA (AHI- 35), 325 w/o OSA (AHI<2)
- Mean age - 60yrs old
- Follow up of 2-4yrs
- Adjusted for age/sex/race, smoking, alcohol intake, BMI, DM, HTN, AF, high cholesterol.

Results

- OSA group - 22 stroke, 50 death
- Control group - 2 stroke, 16 death

Hazard ratio 1.97; (95% CI 1.12-3.48), P=0.01

Yaggi et al, NEJM, 2005

Obstructive Sleep Apnea As A Risk Factor For Stroke: Prospective Cohort Incidence Studies

Study	Type of cohort	N	AHI used to Define OSA group	OSA prevalence	AHI used to define comparison group	Mean follow-up, y	Group outcome	Subjects with outcome, n	OSA as risk factor for outcome (95% CI)
Arzt et al.	Population based	1,189	≥20	7%	< 5	4	Stroke	OSA, 4; comparison, 9	OR, 4.48 (1.31-15.33), P=0.02
Yaggi et al.	Clinic – based	1,022	≥ 5	68%	< 5	3.4	Stroke, TIA, or death	OSA, 72; comparison, 16	HR, 1.97 (1.12-3.48), P=0.01
Redline et al.	Community -based	2462(male)	> 15	44%	≤ 15	8.7	Ischemic stroke	OSA,54; comparison, 31	OR,2.26 (1.45-3.52), P<0.001
			> 19.1	36%	< 4.1	8.7	Ischemic stroke	OSA, 43; comparison, 5	HR, 2.86 (1.10-7.39), P=0.016
		2,960 (female)	>15	24%	≤ 15	8.7	Ischemic stroke	OSA, 37; comparison, 71	OR, 1.65
			> 19.1	18%	< 4.1	8.7	Ischemic stroke	OSA, 25; comparison, 21	HR, 1.21 (0.65-2.24), P=0.695

ACUTE STROKE & SLEEP

- Inversion of sleep-wake rhythm
- Early presence of REM sleep & normal sleep cycle → good prognosis
- Location & extent of stroke determine the disorder
- Neuronal center
 - Peep drive Function
 - Pharyngeal motility
 - Sleep function
- LMS → SDB

Tegmentum Of Pontomedullary

The Major Sleep Disorders Associated With Stroke

Insomnia	Insomnia due to Medical Conditions
Sleep Related Breathing Disorders	Obstructive Sleep Apnea
Hypersomnia	Hypersomnia Of Central Origin not due to a Circadian Rhythm Sleep Disorder, Sleep Related Breathing Disorder, Or Other Cause Of Disrupted Nocturnal Sleep Hypersomnia due to Medical Conditions
Circadian Rhythm Sleep Disorders	Circadian Rhythm Sleep Disorder due to Medical Conditions
Parasomnia	REM Sleep Behavior Disorder
Sleep Related Movement Disorders	Restless Leg Syndrome Periodic Limb Movement Disorder

OTHER PATTERNS OF RESP. DYSFUNCTION

- Apneusis/apnea during sustained inspiration
- Non obstructive apnoea
- OSA/ Mixed apneas
- Failure of automatic breathing (Ondine's curse)
- EDS \longrightarrow Mesencephalic / thalamic strokes
- \downarrow REM sleep \longrightarrow Hemispheric infarction
- Cheyne Stokes respiration \longrightarrow Bil. Hemispheric lesions

OSA IN ACUTE STROKE

- Frequency : 30%- 80%
- AHI >5----- 72%
- AHI>20-----38%
- AHI > 10 in men compared with women(65% vs 48%;
p=0.001)
- AHI>10 with rec. strokes vs. initial Stroke (74% vs. 57.5 ; P-
0.013)

How does the Presence of OSA Affect Stroke Recovery?

- Studies suggest that stroke patients with OSA have
 - Reduce motivation
 - decrease cognitive capacity
 - Prolong rehab stay
 - May increase the risk of recurrent stroke and death.

OSA AS A PREDICTOR OF POOR OUTCOME AFTER STROKE

- ↑ Dependency
- ↑ Post Stroke Mortality
- ↓ Impaired Cognition, Concentration

?MECHANISMS

- Direct effects of ↓ CBF
- Modulation of BP & oxygen saturation with apneic episodes.
- Compromise in perfusion to ischemic penumbra

DIAGNOSIS OF OSA AFTER STROKE

- SATS trial
- PSG → logistical challenges
- Portable devices

TREATMENT OF OSA AFTER STROKE

- CPAP
- Potential to improve recovery
- Reduce risk of recurrence
- ↓ OSA associated HTN, AF, cardiovascular mortality.
- ↓ EDS

? EVIDENCE

- Preliminary RCT of CPAP in AIS:-
- Improvement in stroke scales
- Depressive symptoms
- Motor recovery
- sleepiness

LIMITATIONS

- Inconsistent results
- ? When to initiate CPAP
- Problems with compliance

Lifestyle changes

- Weight loss
- Sleep with head elevated with wedge or pillow
- Avoid sleeping supine
- Avoid alcohol consumption at night

Positive pressure therapy

CPAP or Bilevel devices

TREATMENT OF OSA AFTER STROKE

- CPAP ↓ stroke recurrence
- 7 year → HR 2.897;(95% CI 1.11-7.71) in patients with out CPAP VS CPAP and those without OSA

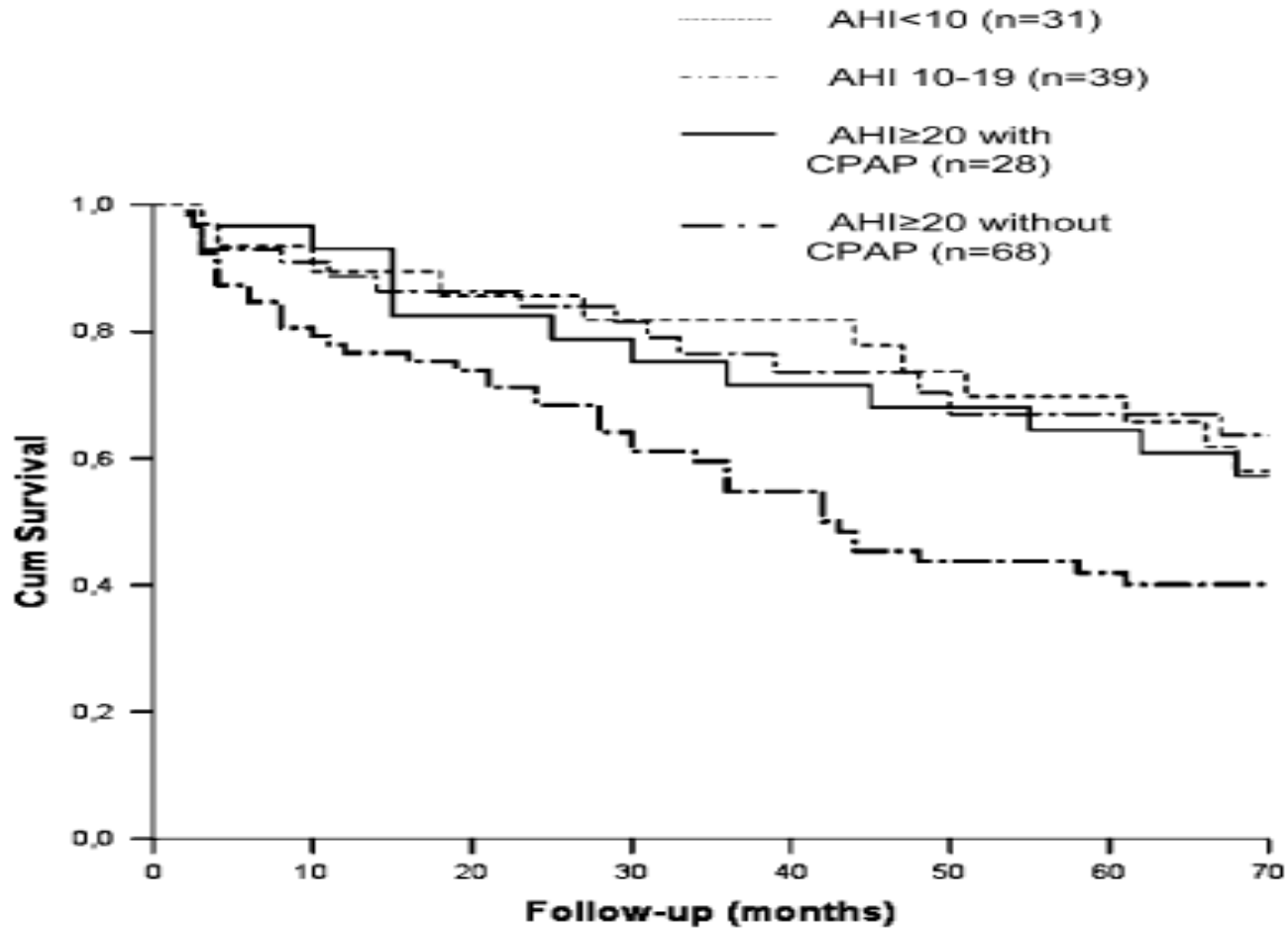


Figure 2. Accumulated survival curve for study groups of patients with stroke, by apnea-hypopnea index (AHI) cutoff point and continuous airway pressure (CPAP) tolerance. The group of patients with stroke with an AHI of 20 or greater and poor tolerance of CPAP showed more mortality than the rest of the patients after 5 years of follow-up. Cum = cumulative.

Use of CPAP and Stroke risk

- Successful treatment of sleep apnea with CPAP lowers blood pressure.
(indirectly lowers the risk of stroke)
- Improves blood flow to the brain
- CPAP therapy reduces mortality, especially after stroke.

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CONCLUSIONS

- Evidence that sleep apnea is a risk factors for stroke is strong & prevalence among stroke survivors is high.
- OSA may be an under appreciated risk factor for poor functional outcome & stroke recurrence.
- How aggressive to pursue a AS of OSA & treatment with CPAP in stroke → evidence is being gathered.
- Current studies through limited suggest that treatment with CPAP may benefit patients after stroke.