Obstructive Sleep Apnea

이 문 규
울산대학교 의과대학 신경과학교실

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- **Definition**
- **Epidemiology**
- **Pathophysiology**
- **Risk factors**
- **Impacts of obstructive sleep apnea**
- **Symptoms**
- **Diagnosis**
- **Treatment**

Sleep-Related Breathing Disorders, ICSD-2 classification

- Central sleep apnea syndromes
- **Obstructive sleep apnea syndromes**
- Sleep-related hypoventilation/hypoxemia syndromes
- Sleep-related hypoventilation/hypoxemia due to medical condition
- Other sleep-related breathing disorders

Definition

- **Obstructive sleep apnea (OSA)**
  수면 중 주기적으로 상기도 저항이 증가하여, 반복적으로 폐쇄 또는 협착이 일어나 무호흡 또는 저호흡이 발생하는 것

- **Obstructive sleep apnea syndrome (OSAS)**
  OSA + clinical symptoms

Prevalence (OSA)

	N	Age (yrs)	RDI > 5 (%)	
			Men	Women
Wisconsin[1]	626	30-60	24	9
Pennsylvania[2]	1741	20-99	17	-
Spain[3]	400	30-70	26	28
Korea[4]	5020	40-69	27	16

(1) Young TB et al., NEJM 1993
(2) Bixler E et al.,Am J Respir Crit Care Med 1998
(3) Duran J et al.,Am J Respir Crit Care Med 2001
(4) Kim J et al.,Am J Respir Crit Care Med 2004

Prevalence (OSAS)

- Adult
- Wisconsin Sleep Cohort Study
  - OSA
    - M/F: 24%/9%
  - OSAS
    - M/F: 4%/2%

- 국내
  - OSA
    - M/F: 27%/16%
  - OSAS
    - M/F: 4.5%/3.2%

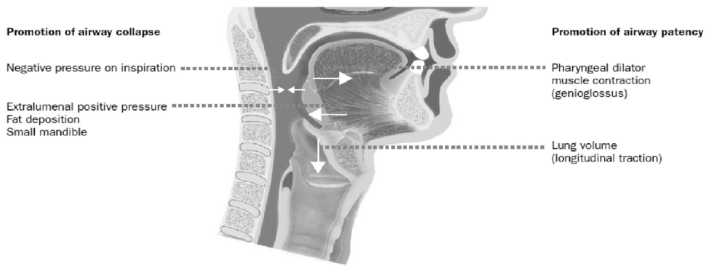
Kim JK et al.,Am J Respir Crit Care Med 2004

Pathophysiology

- Anatomic factors + physiologic factors
  - Anatomic factors
    - Micrognathia, macroglossia, large tonsil, length of upper airway, etc.
  - Physiologic factors
    - Obesity, aging, re-coil properties of airway, etc.
- Influenced by genetic and environmental factors

Sleep Med Rev 2000

Airway patency



Atul Malhotra, David P White, Lancet 2002

Airway patency

- Regulated by
  - Dilator muscle tone
  - Neurogenic control
  - Re-coil properties of airway

Sleep & Airway patency

- **Sleep & upper airway dilator tone**
  - Wakefulness: Dilator tone ↑
  - Sleep: Dilator tone ↓

Malhotra A, Prog Cardiovasc Dis 2009

- **Respiratory control system**
  - During sleep, the central respiratory output waxes and wanes.
  - The periods of low central respiratory drive + decreased dilator muscle activity + high airway resistance + predisposition to airway collapse → apnea

Strohl K, Compr Physiol 2012

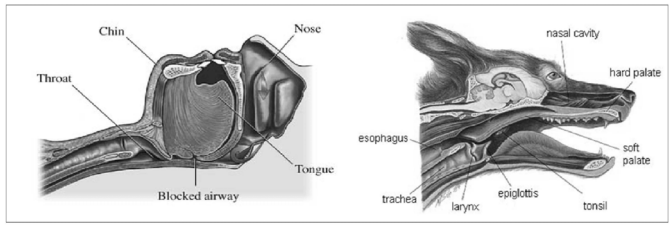
- **Microarousal**
  - Arousal → (transient) hyperventilation → CO_2 ↓ → Dilator muscle activity ↓ → airway collapse

Amy S Jordan, Lancet 2014

Airway patency

- Upper airway lumen/lung volume mismatching
  → increased luminal negative pressure
- Upper airway inflammation (snoring, smoking)
  → loosening of neurogenic control
  → decreased dilator muscle power
- Fluid retention around the upper airway

Handicap



Genetic factors

- Potential phenotypes for OSA
  - Obesity
  - Ventilatory control
  - Craniofacial anatomy
  - Sleep – wake control

Familial Aggregation of OSA

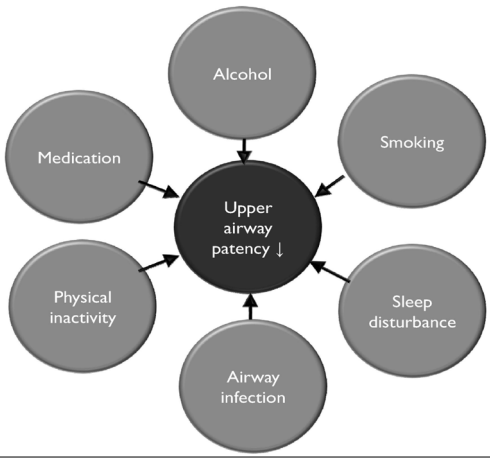
- Familial aggregation of the AHI level and symptoms of OSA

Ann Inern Med 1995, Chest 1990

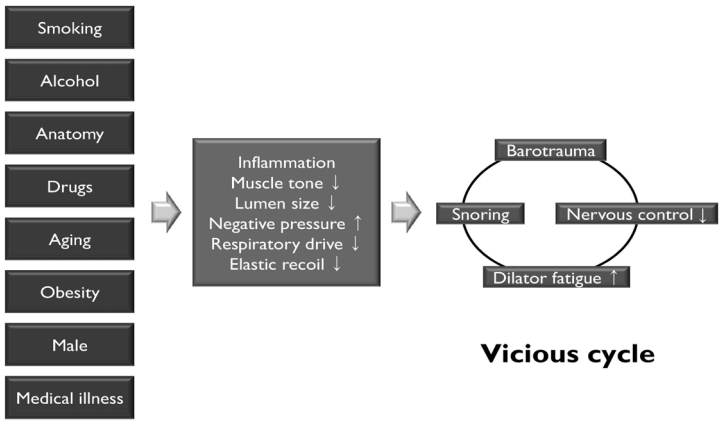
- Twin studies
  - Monozygotic twins > dizygotic twins
  - Concordance rates for snoring
  - Cardinal symptoms of OSA

Sleep 2004, Am J Respir Crit Care Med 2001

Environmental factors



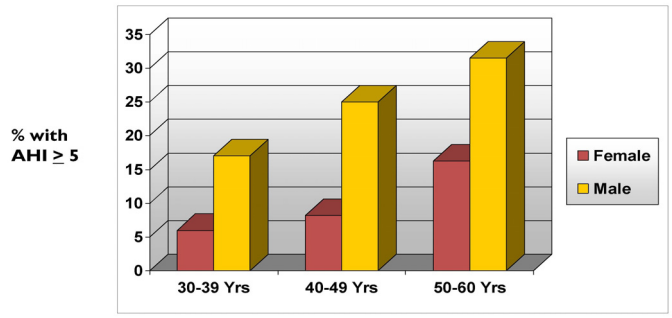
Pathophysiology



Risk factors

- Obesity: m/i
- Neck circumference
  - Western ≥43cm (male 17 inches, female 16 inches)
  - Korean ≥ 40cm
- Craniofacial anatomy
  - Macroglossia, micrognathia
- Alcohol
- Drugs – sedatives, muscle relaxants
- Smoking
- Underlying illnesses
  - Marfan SD, hypothyroidism, etc.

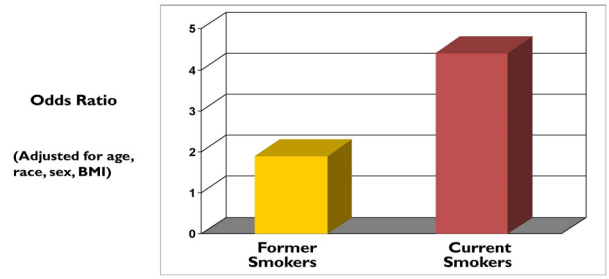
Risk Factor: Age



Young T et al., N Engl J Med 1993

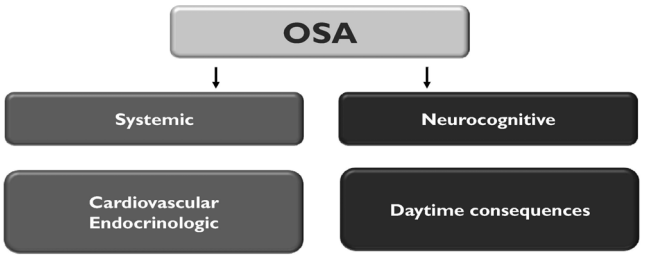
Risk factor: Smoking

Adjusted Odds Ratio for Sleep Apnea (AHI > 15) in Former & Current Smokers vs Nonsmokers



Wetter DW et al. Arch Intern Med 1994

Consequences of OSA



Consequence of OSA
Hypertension

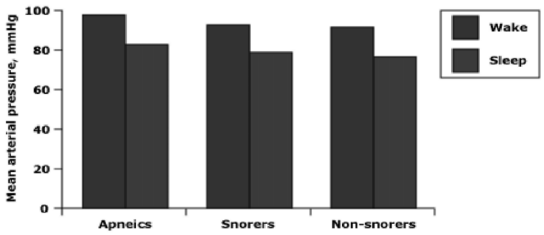
- Hypertension
  - OSA → hypoxemia, increased sympathetic tone → Cardiac output ↑, peripheral resistance ↑
  - 고혈압 환자의 30-83% → OSA
  - **Uncontrolled HTN**에서 AHI ≥ 10

    Logan AG et al., J Hypertens 2001
  - Higher AHI → **uncontrolled HTN** ↑

    Lavie P, Sleep 2001
  - Cohort study: OSA가 있으면, HTN가능성 높다
  - Control: AHI < 5
  - AHI ≥ 5 → OR = 2.74
  - AHI ≥ 15 → OR = 4.54

    Peppard PE, NEJM 2000

Consequence of OSA
Hypertension



Ann Intern Med 1994

Systemic consequence of OSA
Cardiovascular disease

- Heart failure: 12-53%에서 OSA동반
  - Pts with low LVEF (< 45%): Pts with AHI > 10 (53%)

Chest 2005

- A.fib and OSA: OR = 2.19

Circulation 2004

- Coronary Dz
  - Ischemic heart Dz: 30-58%에서 OSA

Eur Respir J 1999, Am J Respir Crit Care Med 2001

Systemic consequence of OSA
Metabolic syndrome

- Metabolic syndrome
  - 146 OSA pts: metabolic SD in 60%
  - 82 non-OSA pts: metabolic SD in 40%
  - Higher AHI → Higher prevalence of metabolic SD

Parish JM, J Clin Sleep Med 2007

  - OSA pts: Insulin resistance ↑

J Appl Physiol 2005

Systemic consequence of OSA
Stroke

- Wisconsin Cohort Study
  - AHI < 5 vs AHI ≥ 20
  - Adjusted for age & sex: OR = 4.48
  - Adjusted for age, sex, & BMI: not significant

Arzt M et al., Am J Respir Crit Care Med 2005

- Yale Center for Sleep Medicine Cohort Study
  - OSA환자의 hazard ratio: 1.97
  - AHI가 심할수록 위험성 증가

Yaggi HK et al., NEJM 2005

- OSA가 stroke의 위험인자로 작용할 가능성은 있다. (Evidence leve Iib, Stroke 2006)

Systemic consequence of OSA
Stroke

As a risk factor

- Cerebral infarction was significantly associated with habitual snoring
- Risk ratio of **10.3** (95% CI, 3.5-30.1)

M Partinen and H Palomaki, Lancet 1985

- Habitual snoring carries a significant risk factor for stroke (odds ratio: **2.9**, 95% CI 1.3 to 6.8 (p = 0.01)).

Neau JP et al., Acta Neurol Scand 1995

- Relative risk; 1.26-10.3

Systemic consequence of OSA
Stroke

- **Less well-documented or potentially modifiable risk factors**
  - Metabolic syndrome
  - excessive alcohol consumption
  - drug abuse
  - oral contraceptives
  - **sleep-disordered breathing**
  - Migraine
  - Hyperhomocysteinemia
  - elevated lipoprotein
  - Hypercoagulability
  - Inflammation
  - Infection.

Guideline from AHA/ASA 2011

Time course of sleep-disordered breathing in ischemic stroke

N=161

During acute phase

- 116 of 161 (71.4%) pts had AHI > 10/hr
- 45 of 161 (28%) had AHI > 30/hr
- 42 of 161 (26.1%) had Cheyne-Stokes breathing.

During stable phase (3 mo. after stroke)

- 53 of 86 (61.6%) had AHI >10/hr
- 17 of 86 (19.8%) had AHI > 30/hr

Parra O et al., Am J Respir Crit Care Med 2000

Location of stroke and OSA; still uncertain

- Sleep apnea as a features of bulbar stroke
- Obstructive sleep apnea after lateral medullary infarction
- No relationships were found between sleep-related respiratory events and the topographical parenchymatous location of the neurological lesion or vascular involvement.

Parra O et al., Am J Respir Crit Care Med 2000

Relationship between OSA & stroke

- Bi-directional relationship
  - OSAS is an emerging cause as an important risk factor for ischemic strokes
  - SDB could be a consequence of strokes
    - Complication
    - Drugs
    - Involvemen of
      - pontomedullary reticular formation
      - nucleus tractus solitarius

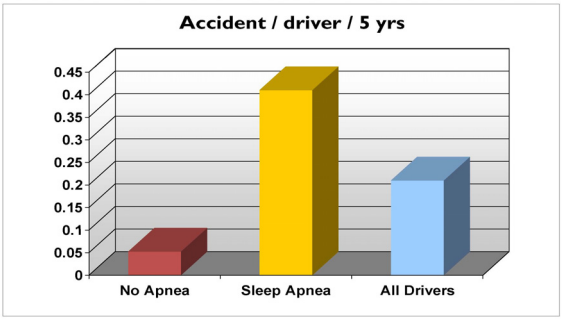
Consequence of OSA
Cognitive dysfunction

- 결과가 다양
  - attention, motor coordination, executive function: decreased
  - IQ, language function: not impaired
- Vehicle accidents
  - OSA환자의 교통사고 발생율: 1.21~4.89

    Tregear S et al., J Clin Sleep Med 2009
  - CPAP → 사고 감소

    Antonopoulos CN, Sleep Med Rev 2010

Consequence of OSA
Cognitive dysfunction



Findley LJ et al., Am Rev Respir Dis 1988

Consequence of OSA
Headache

- OSA환자에서 두통: 15~60%
- 31 of 25 Cluster headache pts had OSA

  Graff-Radford SB, Headache 2004
- ICHD-2: headache attributed to disorder of homeostasis
  - A. Recurrent headache with at lease one of the following characteristics and fulfilling criteria C and D:
    1. Occurs > 15 times/month
    2. Bilateral, pressing quality and not accompanied by nausea, photophobia or phonophobia
    3. Each headache resolves within 30 min
  - B. Sleep apnea demonstrated by overnight PSG
  - C. Headache is present upon awakening
  - D. Headache ceases within 72 hr, and does not recur, after effective treatment of sleep apnea

Consequence of OSA
Headache

- Hypoxemia, hypercapnea → disturbing autoregulation
- Excessive neck motion
- Increased muscle activity
- Sleep fragmentation

Consequences of OSA

Panel 1: **Consequences of obstructive sleep apnoea**

Effect	Magnitude (odds ratio)	Reference
Neurocognitive		
Motor vehicle accidents	7	Teran-Santos[1]
Occupational accidents	2·2	Lindberg[16]
Cardiovascular		
Prevalent hypertension	1·4	Nieto[6]
Incident hypertension	2·9	Peppard[8]
Coronary disease	1·3 to 23	Shahar, Hung[5,122]
Stroke	1·6	Shahar[5]
Congestive heart failure	2·4	Shahar[5]

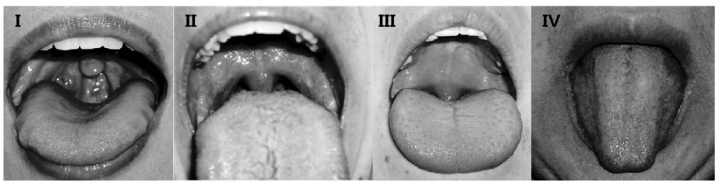
Atul Malhotra, David P White, Lancet 2002

Clinical Signs & Symptoms

- Snoring
- Witnessed apnea
- Excessive daytime sleepiness
- Morning headache
- Dry throat in the morning
- Depressive symptoms
- Erectile dysfunction
- Insomnia
- Impaired vigilance and memory
- Non-refreshing sleep

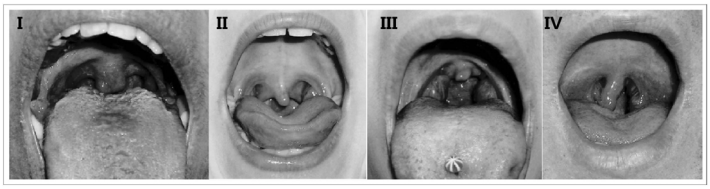
Physical examination

Mallampati classification



소리를 내지 않고, 입을 최대한 크게 벌리고, 혀를 최대한 바깥쪽으로 내민다.

Friedman Tonsil Size



Evaluation

- Daytime sleepiness scale
  - Epworth Sleepiness Scale (ESS): 0-24
    - 0-9: considered to be normal
    - **10**-24: needs expert medical advice

Johns MW, Sleep 1991

Diagnosis

- Overnight PSG: **standard**
  - Electroencephalogram (EEG)
  - Electrooculogram (EOG)
  - Electromyogram (EMG)
  - Electrocardiogram (ECG)
  - Oronasal airflow
  - Chest wall effort
  - Snore microphone
  - Pulse oximetry

Diagnostic criteria of OSAS in adult

A, B and D or C and D satisfy the criteria

A. At least on of the following applies:
1. The patient complains of unintentional sleep episodes during wakefulness, daytime sleepiness, unrefreshing sleep, fatigue, or insomnia.
2. The patient wake with breath holding, gasping, or choking.
3. The bet partner reports loud snoring, breathing interruptions or both during the patient's sleep.

B. Polysomnographic recording shows the following:
1. Five or more scoreable respiratory events (i.e., apnea, hypopneas, or RERAs) per hour of sleep.
2. Evidence of respiratory effort during all or a portion of each respiratory event
(in the case of a RERA, this is best seen with the use of esopheageal manometry.)

Or

C. Polysomnographic recording shows the following:
1. Fifteen or more scoreable respiratory events (i.e., apneas, hypopneas, or RERAs) per hour of sleep.
2. Evidence of respiratory effort during all or a portion of each respiratory events.
(in the case of a RERA, this is best seen with the use of esophageal manometry.)

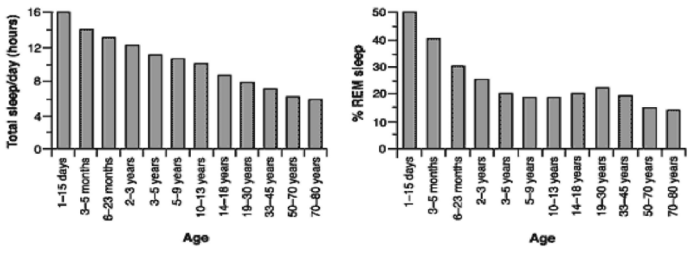
D. The disorder is not better explained by another sleep disorder, medical or neurological disorder, medication use, or substance use disorder.

ICSD-2, AASM 2005

Normal Sleep Pattern

	Infant	Adult	Elderly
WASO	< 5%	< 5%	10-20%
Sleep efficiency	> 90%	> 90%	80-85%
Stage N1		2-8%	4-10%
Stage N2		45-55%	35-45%
Stage N3		13-23%	5-18%
Stage R	50%	20-25%	15-20%
REM/NREM ratio	50:50	20:80	20:80
REM:NREM cycle	45-60 min	90-110 min	90-110 min
Total sleep time	14-16 hrs	7-8 hrs	7 hrs

Normal Sleep Pattern



Data from Roffwarg, H.P., J.N. Muzio, and W.C. Dement. 1966. Ontogenetic development of the human sleep-dream cycle. *Science*, 152: 604–619.

Measuring Airflow

- Thermal sensor
  – for apnea
- Pressure Transducer (PTAF)
  – for hypopnea

Measuring Respiratory Effort

- Esophageal manometry
  - Gold standard

- Inductance Plethysmography
  - Preferred

Apnea Scoring

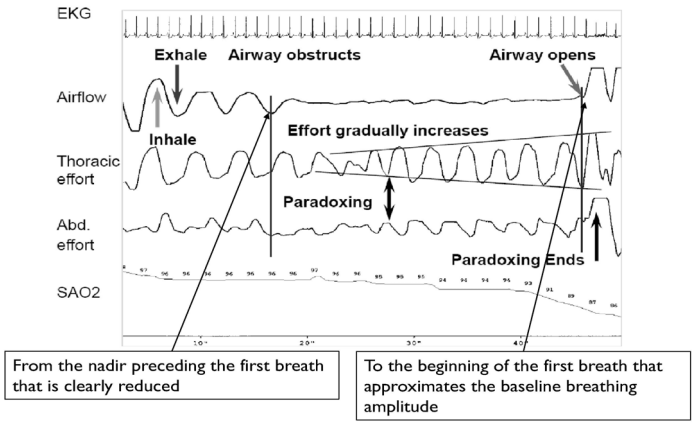
- All of the following criteria are met (by thermal sensor):
  - ≥ 90% fall in the amplitude for ≥ 90% of the event's duration
  - ≥ 10 seconds in the duration

Note: no desaturation or arousal criteria.

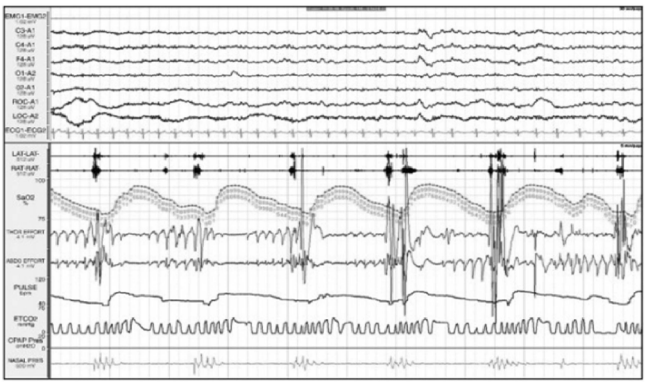
- Classify an apnea in an adult based upon inspiratory effort

1. Obstructive apnea
   Apnea critera + continued or increased inspiratory effort
2. Central apnea
   Apnea criteria + absent inspiratory effort
3. Mixed apnea
   Apnea criteria +
   absent inspiratory effort (initial) + resumption of inspiratory effort (following)

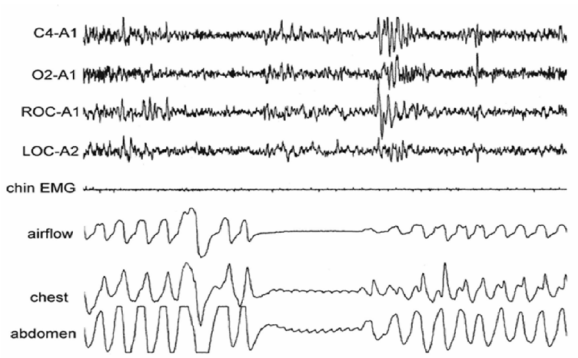
Obstructive apnea



Mixed apnea



Central apnea



Hypopnea scoring

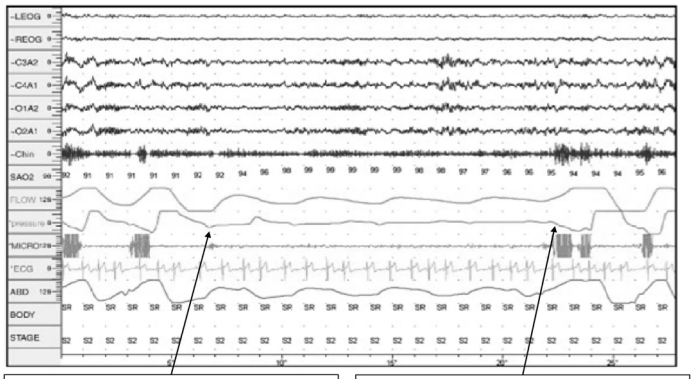
All of the following criteria are met (by pressure sensor):
(Recommended)

1. ≥ 30% fall in the amplitude
2. ≥ 10 seconds in the duration
3. ≥ 4% desaturation
4. ≥ 30% fall in the amplitude for ≥ 90% of the event's duration

(Alternative)

1. ≥ 50% fall in the amplitude
2. ≥ 10 seconds in the duration
3. ≥ 3% desaturation
4. ≥ 50% fall in the amplitude for ≥ 90% of the event's duration

Hypopnea

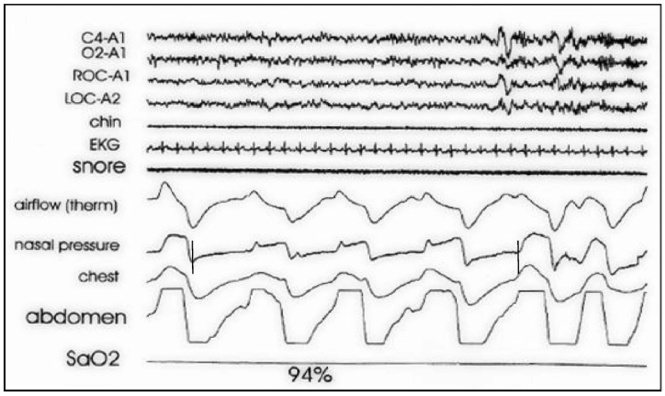


RERA scoring

- When the following are met:
  1. ≥ 10 seconds in the duration
  2. Increasing respiratory effort or flattening of the nasal pressure waveform
  3. Arousal
  4. Not meet criteria for an apnea or hypopnea

- *Note*
  Esophageal pressure (perferred)
  Nasal pressure (can be used)

RERA



Severity of OSA

- Severity criteria
  - AHI
    - Mild: 5-14
    - Moderate: 15-29
    - Severe: ≥ 30

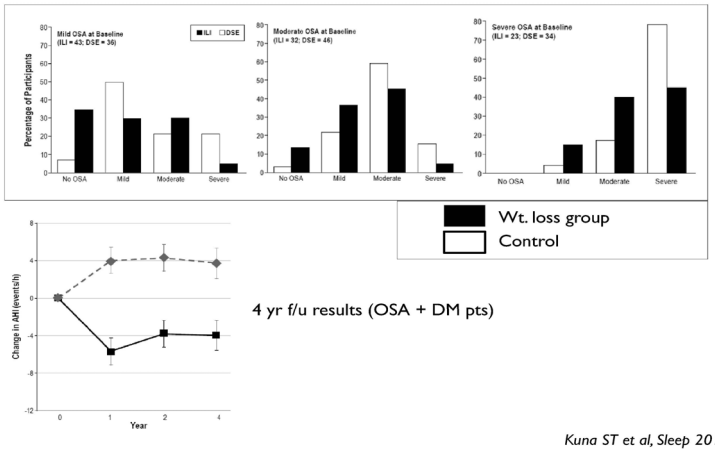
Sleep disordered breathing

- Snoring
- Upper airway resistance syndrome (UARS)
  - An obsolete term used to define increased RERA but with AHI < 5. the current definition subsumes UARS under the OSA category
- Obstructive sleep apnea syndrome

Behavioral Methods

- Weight loss
- Avoid alcohol, smoking, and sedatives
- Avoid sleep deprivation
- Avoid supine sleep position

Weight loss



4 yr f/u results (OSA + DM pts)

Kuna ST et al, Sleep 2013

Weight loss

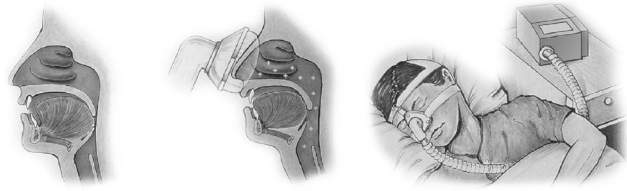
- 10 – 15 % reduction in weight can lead to an approximately 50 % reduction in sleep apnea severity in moderately obese male patients.

Drug treatments

- REM reduction, increased respiratory drive, improve daytime sleepiness
  - TCA (protriptyline, paroxetine)
  - Provigil for somnolence

**No drugs were approved for OSA treatment*

Continuous Positive Airway Pressure (CPAP)



AASM recommendation
- Moderate to severe OSA (standard)
- Mild OSA (option)
- Improving self-reported sleepiness in patient with OSA (standard)
- Improving QoL in patients with OSA (option)
- Adjunctive therapy to lower blood pressure in HTN with OSA (option)

Continuous Positive Airway Pressure (CPAP)

- Moderate to severe OSA의 gold standard
- Treatment goal: elimination

- Titration
  - From 4 cmH_2O ~ 20 cmH_2O (adult)

Acceptable titration		
Optimal	Good	Adequate
RDI < 5 SpO2 > 90% Acceptable leak At least a 15 min duration including supine REM sleep that is not continually interrupted by spontaneous arousals or awakenings	RDI < 10 or RDI < 15 and reduced by 50% from baseline + supine REM sleep	Not reduced RDI ≤ 10 but reduced 75% from baseline Meets the criteria for optimal or good with no supine REM data

Continuous Positive Airway Pressure (CPAP)

- 단점
  - Poor compliance
  - Long-term adherence rate: 40~80%

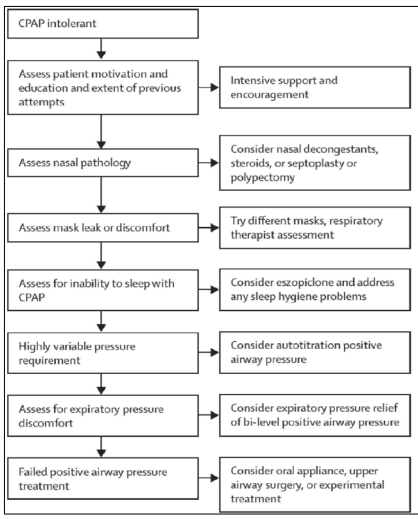
- Side effects
  - 구강/인두 점막 건조, 눈충혈 (air leak), 소음, 답답함
  - Skin abrasions, rashes

Alternatives for CPAP

- AutoPAP
- BiPAP
- Adaptive servo-ventilation

CPAP adherence

- Use of the CPAP device: > 4hr/night for > 70% of nights/month
- For improving adherence
  - Different interface optioins, different device, addition of humidity, intensive education, close f/u, treatment of nasal congestion, transient BZD to sleep induction
- Prediction for long-term adherence
  - Symptom improvements
  - More severe OSA, more higher adherence
  - Excessive daytime sleepiness
  - Subjective satisfaction



잘 설명해주고
Mask종류도 바꿔보고
비/인두의 해부학적인 문제가 있으면 교정도 해주고
장비도 바꿔보고
Oral appliance도 사용해 보고

Amy S Jordan, Lancet 2014

Surgery

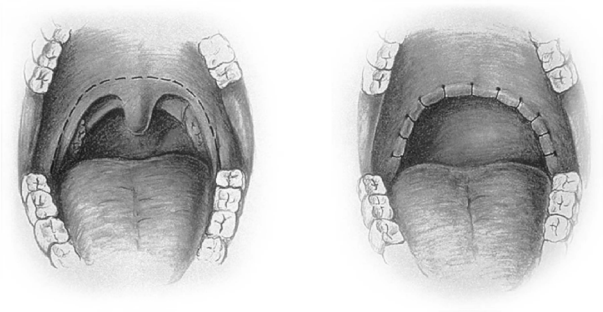
- UPPP
- S/E: pain, nasal reflux, nasal speech, palatal stenosis
- Successful surgery
  - Postsurgical RDI < 20 or reduction more than 50%
  - Postsurgical SaO2 > 90%
  - Normalization of sleep architecture
  - Improvements of daytime sleepiness
- 수술적 치료는 CPAP에 적응하지 못하고, 해부학적인 문제가 있는 환자에게서 선택적으로…..
- Surgical treatment should be considered in sleep apnea patients who use CPAP inadequately

Otolaryngol Head Neck Surg 2004

Surgical Methods

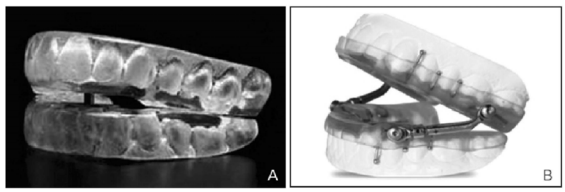
- Reconstruct upper airway
  - Uvulopalatopharyngoplasty (UPPP)
  - Laser-assisted uvulopalatopharyngoplasty (LAUP)
  - Radiofrequency tissue volume reduction
  - Genioglossal advancement
  - Nasal reconstruction
  - Tonsillectomy
- Bypass upper airway
  - Tracheostomy

Uvulopalatopharyngoplasty (UPPP)



Oral appliance

- Mandibular advancement device (MAD)
  - Mild에 효과적.
  - Success rate: 50%



Summary

- Prevalence of OSA: high
- Progressive worsening: snoring → OSAS
- Cardiovascular/Endocrinologic/Neurocognitive Cx.
- Diagnosis: overnight PSG
- Treatment: CPAP + behavioral + etc.