



Obesity Hypoventilation Syndrome (OHS)

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Definition

Table 1—*Definition of OHS*

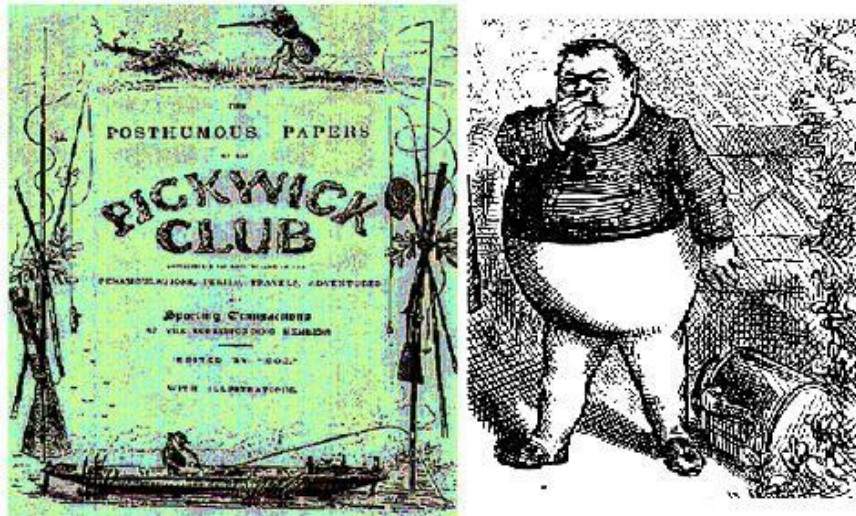
Required Conditions	Description
Obesity	BMI ≥ 30 kg/m ²
Chronic hypoventilation	Awake daytime hypercapnia (PaCO ₂ ≥ 45 mm Hg)
Sleep-disordered breathing	OSA (AHI ≥ 5 with or without sleep hypoventilation) present in 90% of cases; <u>sleep hypoventilation</u> (AHI < 5) present in 10% of cases
Exclusion of other causes of hypercapnia	Severe obstructive airways disease; severe interstitial lung disease; severe chest wall disorders (<i>eg</i> , kyphoscoliosis); severe hypothyroidism; neuromuscular disease; and congenital central hypoventilation syndrome

■ ***sleep hypoventilation*** is defined as

- an increase in Paco₂ during sleep by 10 mm Hg above wakefulness or
- a significant oxygen desaturation that is not explained by obstructive apneas or hypopneas

History

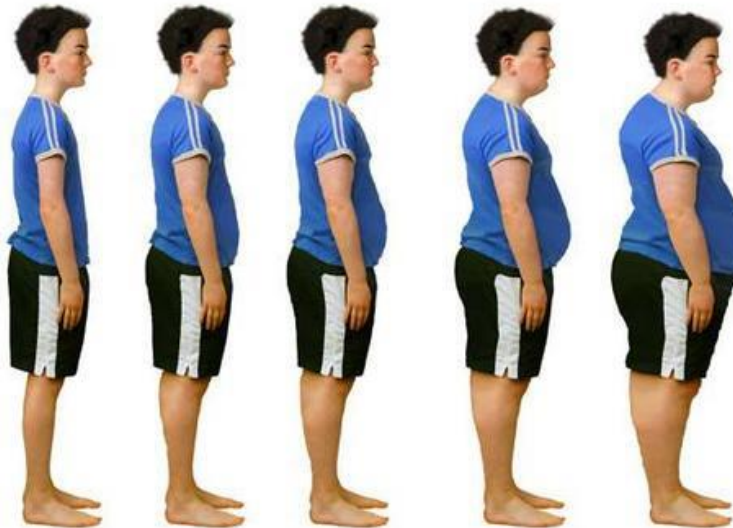
- Obesity hypoventilation syndrome was classically described as → “Pickwickian syndrome” in a 1956 case report by Burwell
- This patient resembled a character depicted by Dickens in his story, *The Posthumous Papers of the Pickwick Club*, because both were obese with excessive hypersomnolence.



Front wrapper from The posthumous paper of the Pickwick Club by Charles Dickens and drawn of Joe

Obesity

- In the United States,
 - 1/3 of the adult population is obese
 - the prevalence of extreme obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$) is increasing rapidly
- From 1986 to 2000, the prevalence of
 - $\text{BMI} \geq 40 \text{ kg/m}^2$ – increased by fourfold
 - $\text{BMI} \geq 50 \text{ kg/m}^2$ – increased by fivefold



Freedman DS, Khan LK, Serdula MK, et al. Trends and correlates of class 3 obesity in the United States from 1990 through 2000. JAMA 2002; 288:1758–1761

Sturm R. Increases in clinically severe obesity in the United States, 1986–2000. Arch Intern Med 2003; 163:2146–2148

Obesity

- The obesity epidemic is not only impacting adults in the United States,
→ it is a global phenomenon affecting children and adolescents
- With such a global epidemic of obesity,
→ the prevalence of OHS is likely to increase

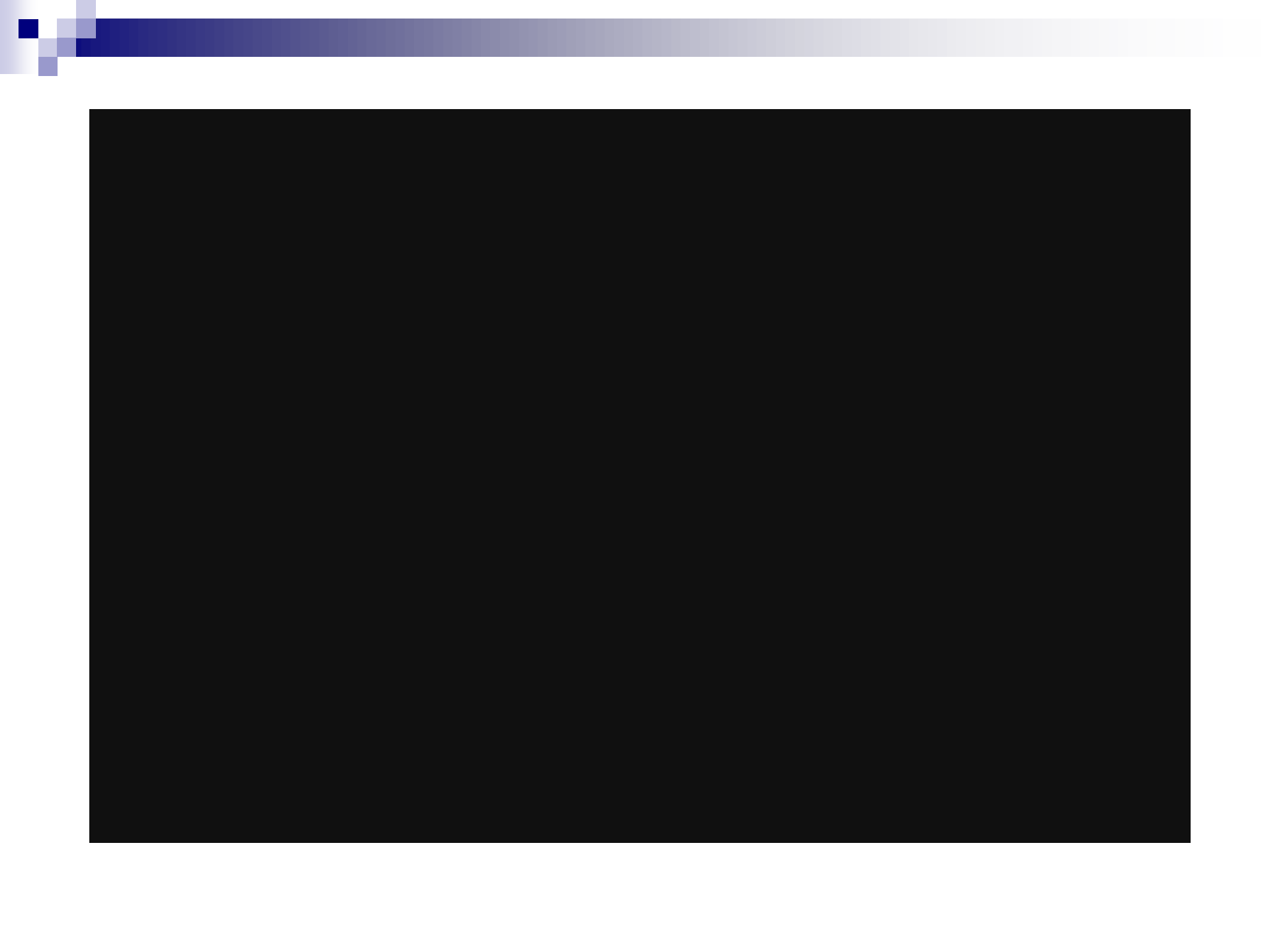


Prentice A, Webb F. Obesity amidst poverty. *Int J Epidemiol* 2006; 35:24–30

Skidmore PM, Yarnell JW. The obesity epidemic: prospects for prevention. *Q J Med* 2004; 97:817–825

Spritzer DA. Obesity epidemic migrates east [letter]. *Can Med Assoc J* 2004; 171:1159

Miech RA, Kumanyika SK, Stettler N, et al. Trends in the association of poverty with overweight among US adolescents, 1971–2004. *JAMA* 2006; 295:2385–2393



Case

- **Sex/age : F/58**
- **Chief complaint : Known **sleep apnea**, **headache**, Severe **EDS** with mental confusion**
- **Present illness :**

She was admitted at local hospital d/t **pneumonia at 2005.05** but **Respiratory failure** was developed and she **transferred out to one of the university Hospital**. And then **Intubation** was performed.

She was admitted on ICU for **3wks**

Case Cont.

- **Present illness cont. ;**

She said that she **snored & had apnea with severe EDS**. Polysomnography was done at that time. After discharge until now, she received 2 liter of **oxygen therapy only** via nasal cannular **without PAP (Positive Airway Pressure) treatment**.

She was admitted to local **ICU several times** for **CO₂ narcosis with respiratory failure** while she received **2 liter of O₂** via nasal cannular without PAP treatment since 2005 to May, 2007.

She was referred to Korea university SDB center for **further evaluation and treatment** of sleep related breathing disorders on **October, 2007**.

Past History

- HTN/DM/TB/HBV (-/-/-/-)
- ADM/Op Hx(+/+): **Pneumonia ??** [2005],
Admitted **to ICU** for several times since 2005
until 2007 for **CO2 Narcosis**
- Alcohol : none
Smoking : none
- Occupation : housewife

Review of system

- Weight loss/gain(-/-)
- General weakness(-)
- Headache/Dizziness(+/-)
- Daytime sleepiness(+)
- Snoring(+)
- Fever/Chilling(-/-)
- A/N/V/C/D(-/-/-/-/-)
- Wt gain(+)
- C/S/R(-/-/-)
- Chest pain/ Dyspnea on exertion(-/+)
- Apnea on sleeping(+)
- Abdominal pain/discomfort(-/-)
- Urinary Sx(-)

Physical Examination

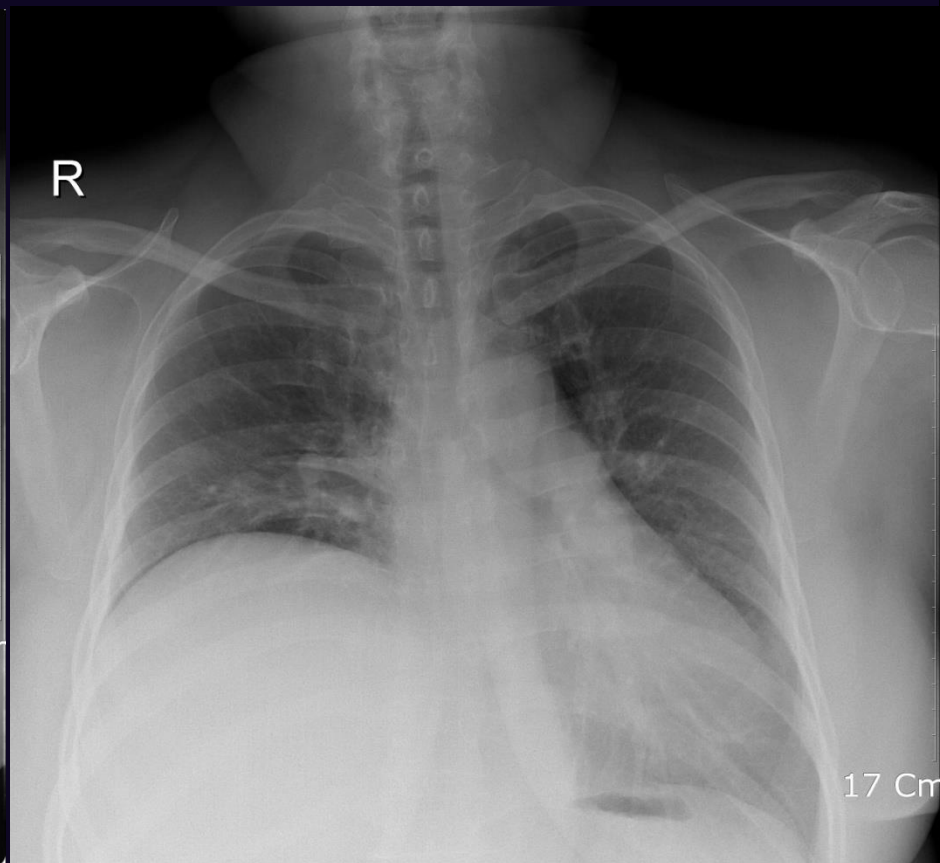
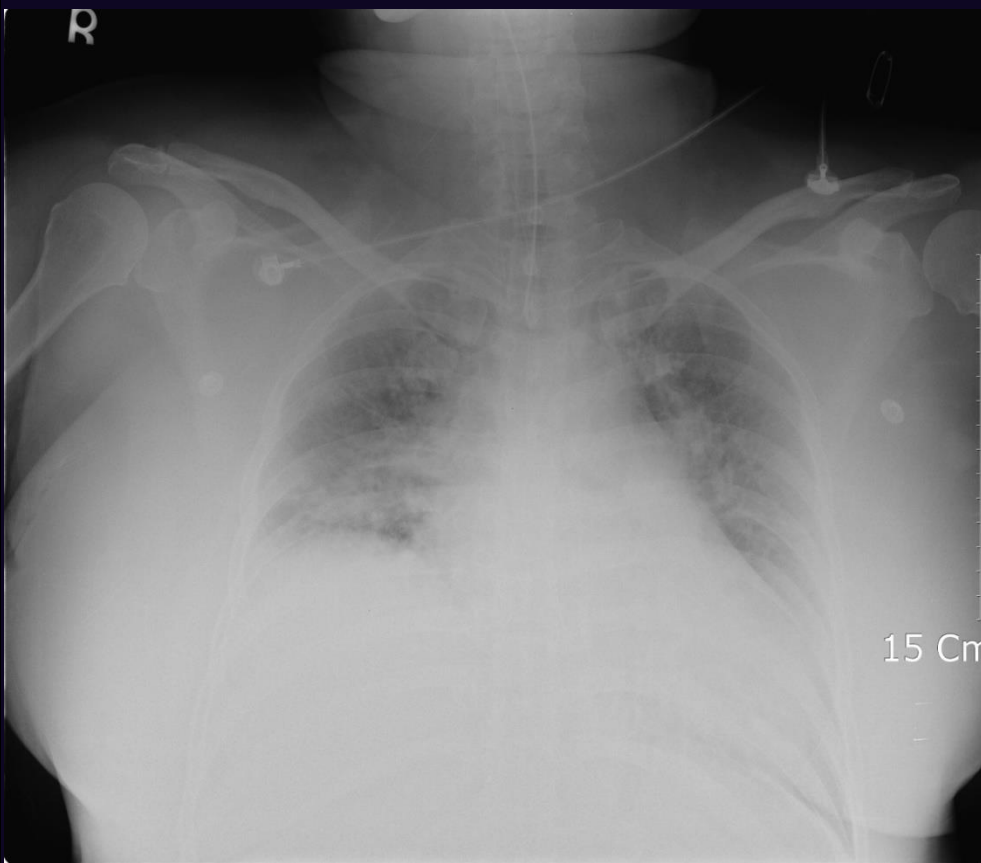
- wt 84.5kg ht 1.53m BMI 36.9kg/m²
- V/S: BP 113/68 PR:72 RR:20 Temp: 36.6 °C
- Mental **drowsy**, but cooperative, **Cyanotic**
- Isocoria c L/R(++/++)
- Not Anemic conjunctiva, Not Icteric sclera
- Regular HB s(m)
- Symmetric Lung Expansion s retraction
- **BLL field → decreased lung sounds** wheezing, crackle
- normal ABS, Abdominal Td/RT(-/-)
- Hepatomegaly(-), splenomegaly(-)
- Pitting edema(-)

Laboratory Finding

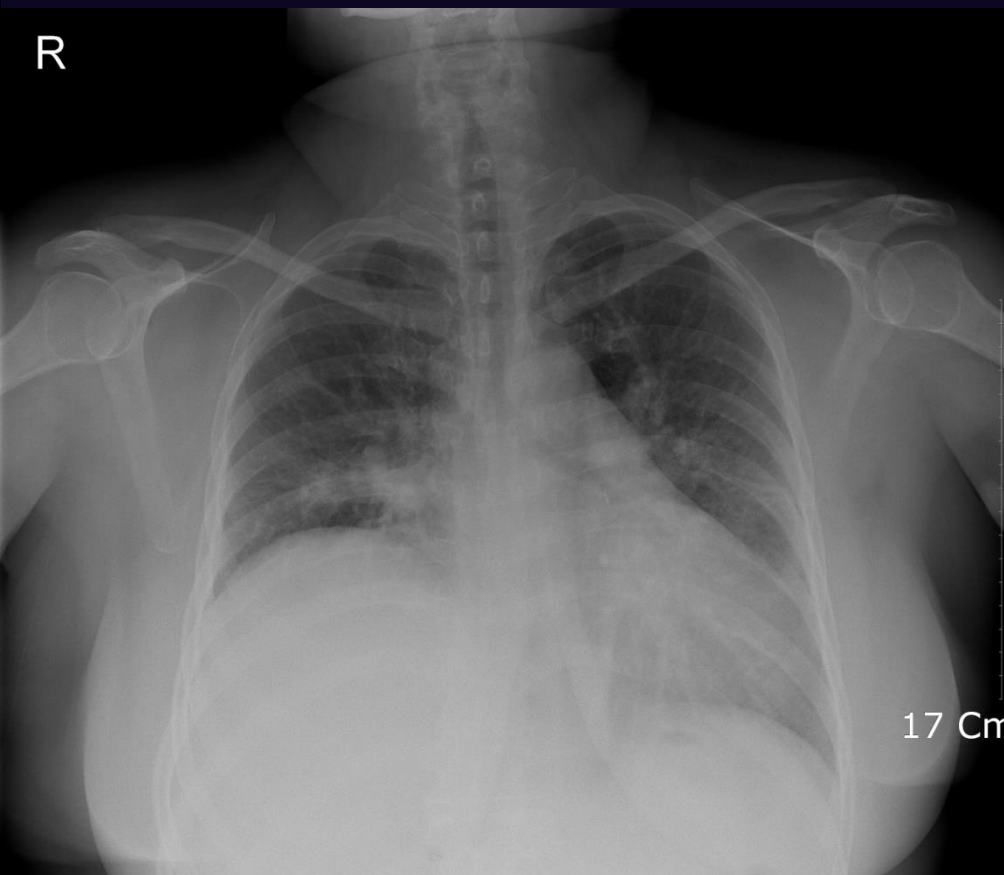
- **Hb : 18.1g/dL, Hct: 59.9%**
- **WBC : 4340/uL(diff neut 51.7%, lymph 34.8%,
mono 8.9%, Eosi 1.9%, baso 0.2%)**
- **Plt, Na-K-Cl(mmol/L), BUN/Cr, AST/ALT ,T-Bil : W.N.L**
- **ABGA at room air) :**
pH 7.297- **pCO₂ 94.9mmHg** - **pO₂ 42.2 mmHg**
HCO₃- 43.5 mmol/L- O₂ saturation 72.5%
- **TFT: W.N.L**
- **Neck and Brain MRI/ CT, Abd. sono : W.N.L**
- **2-D echo (+ m-mode + doppler)**
 - **Grade 1 diastolic dysfunction**
 - **Mild pulmonary hypertension**
(pulmonary arterial pressure: **38mmHg**)
 - **LVEF => Normal**

CXR 2005.05

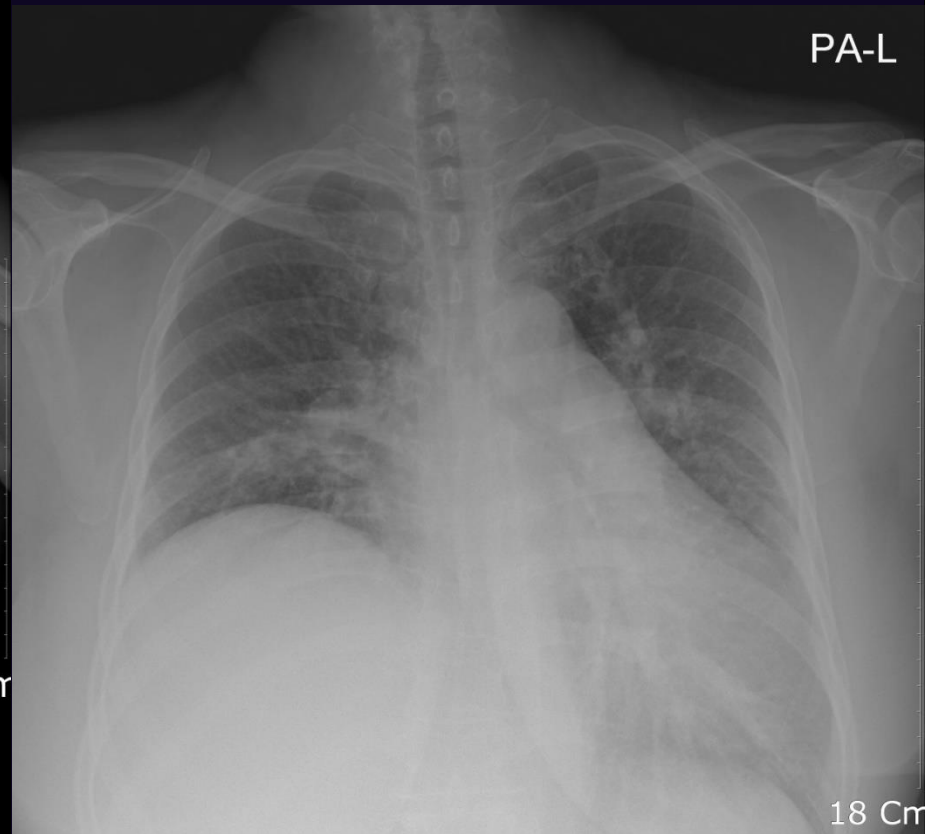
2005.07



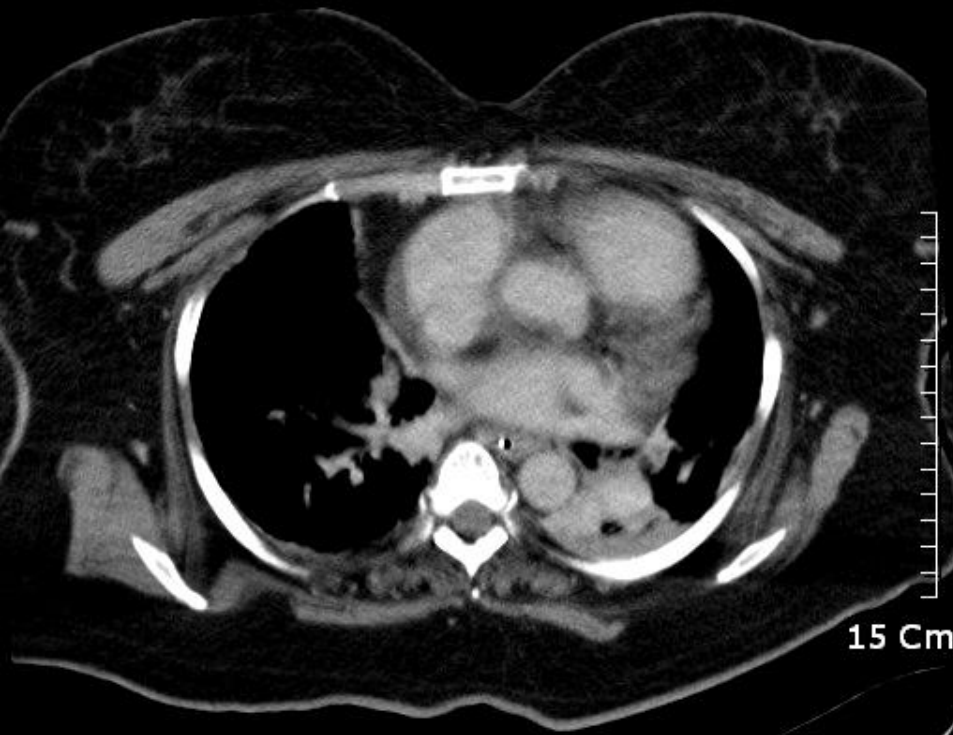
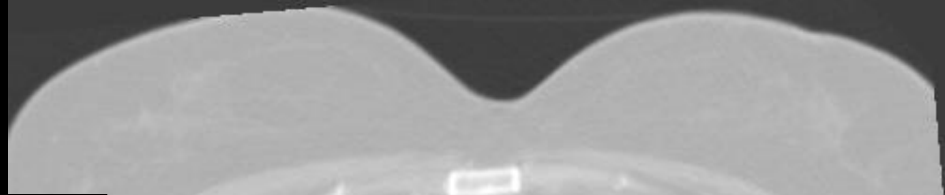
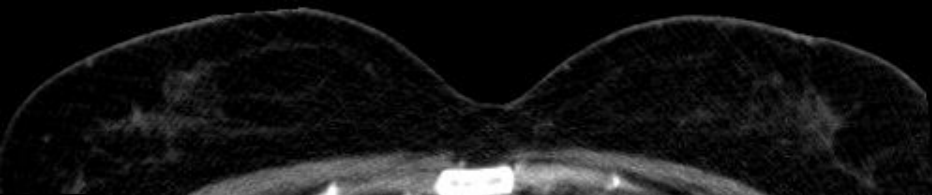
CXR 2006.08



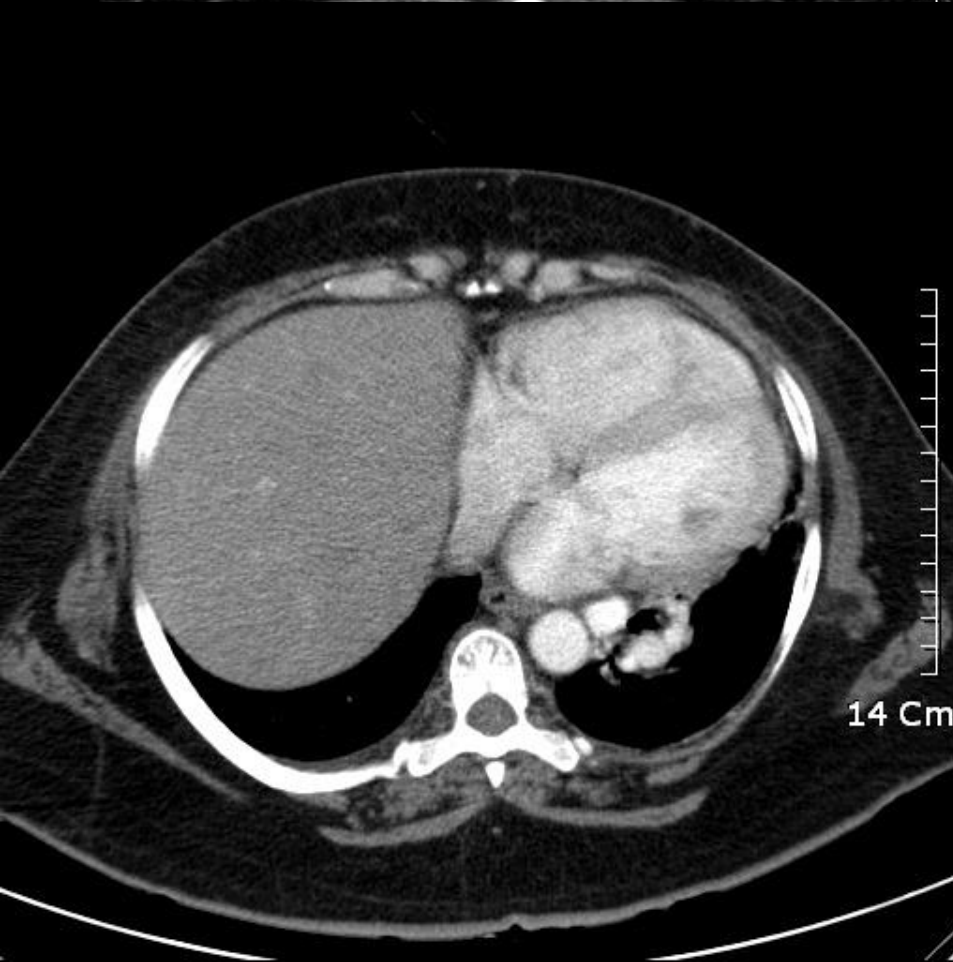
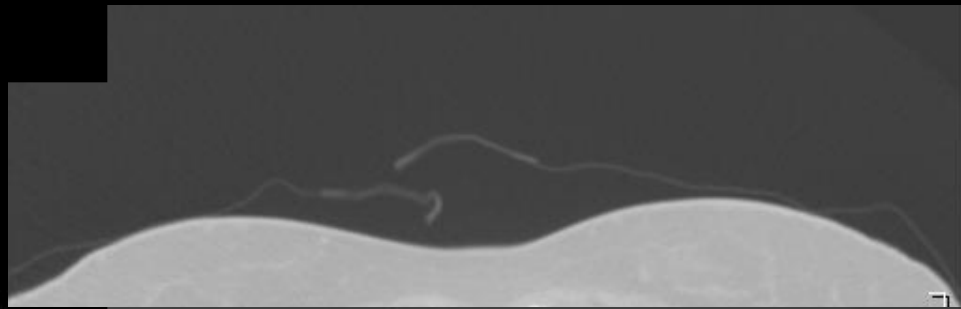
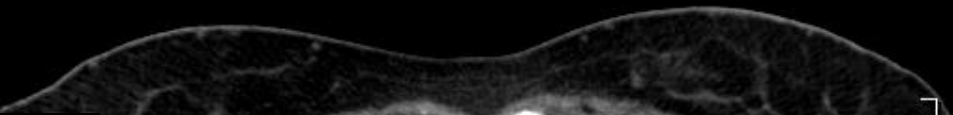
2007.10



Chest CT (2005.05)



Chest CT (2007.10)

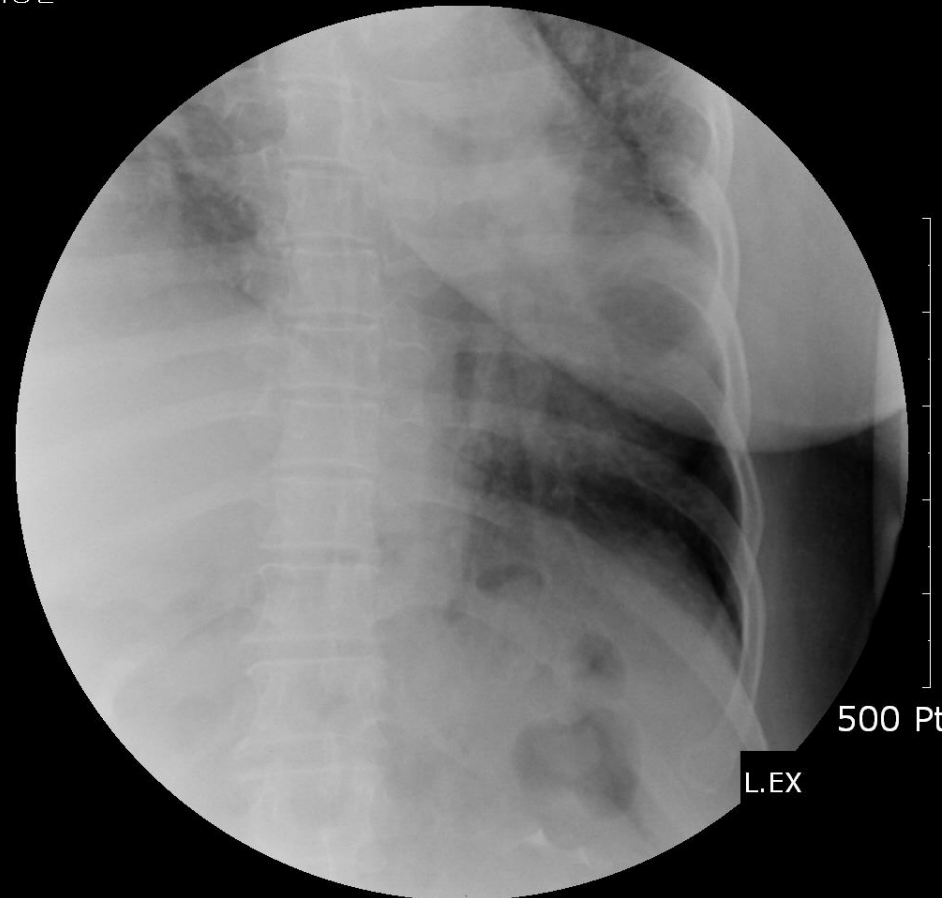
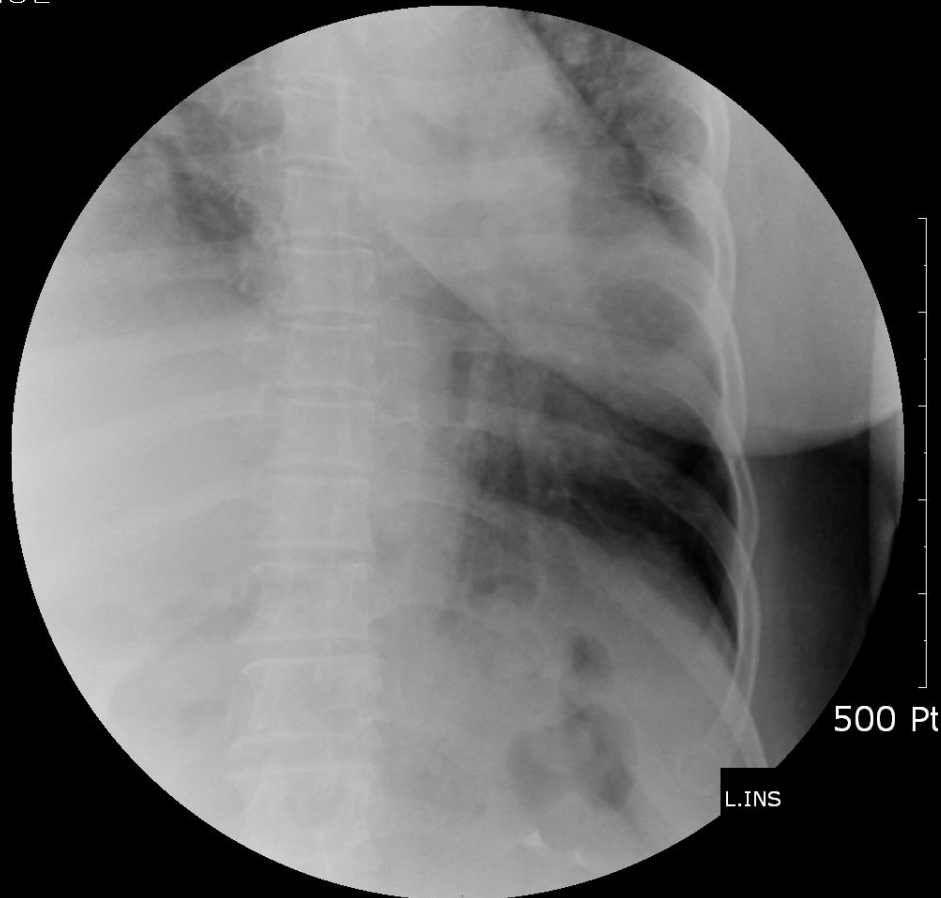


Sniff test

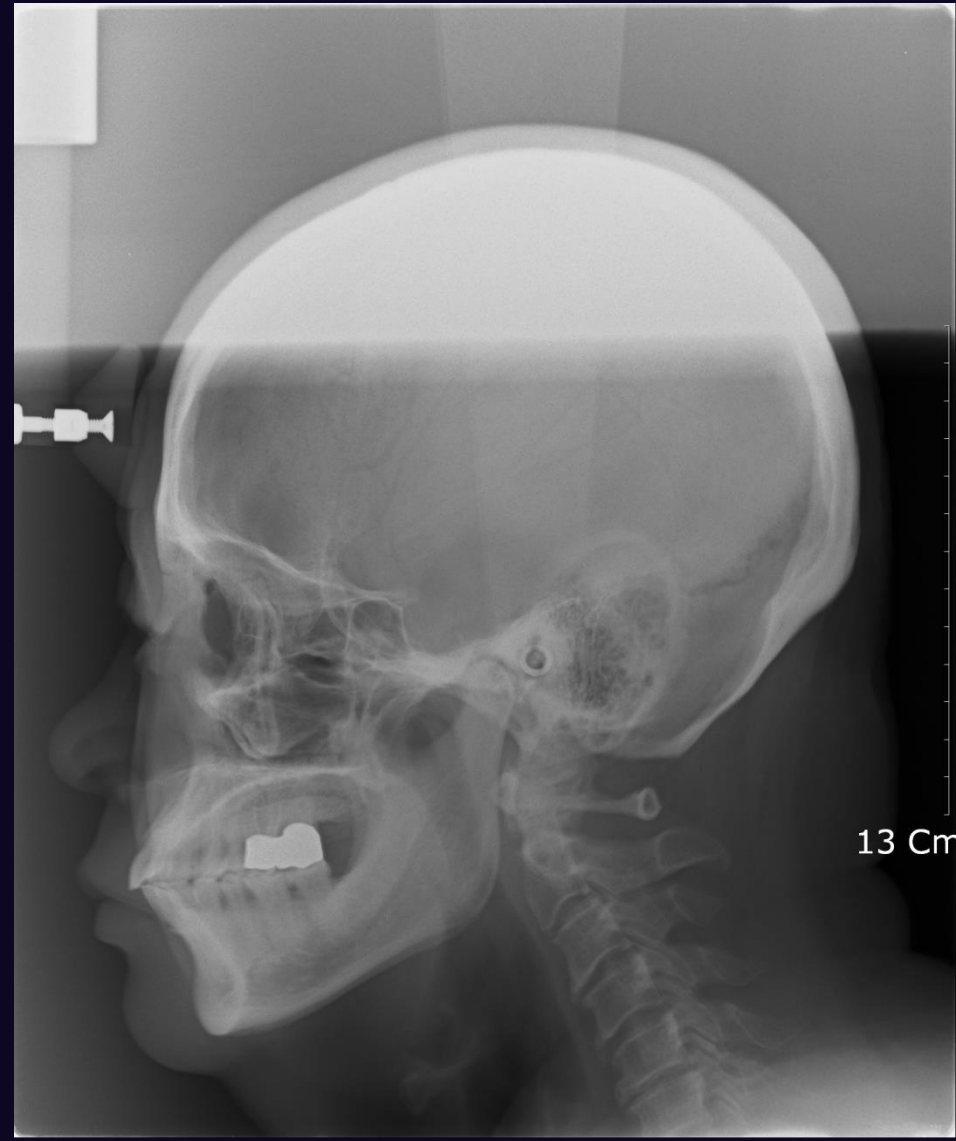
(Rt) side diaphragmatic paralysis

이경순

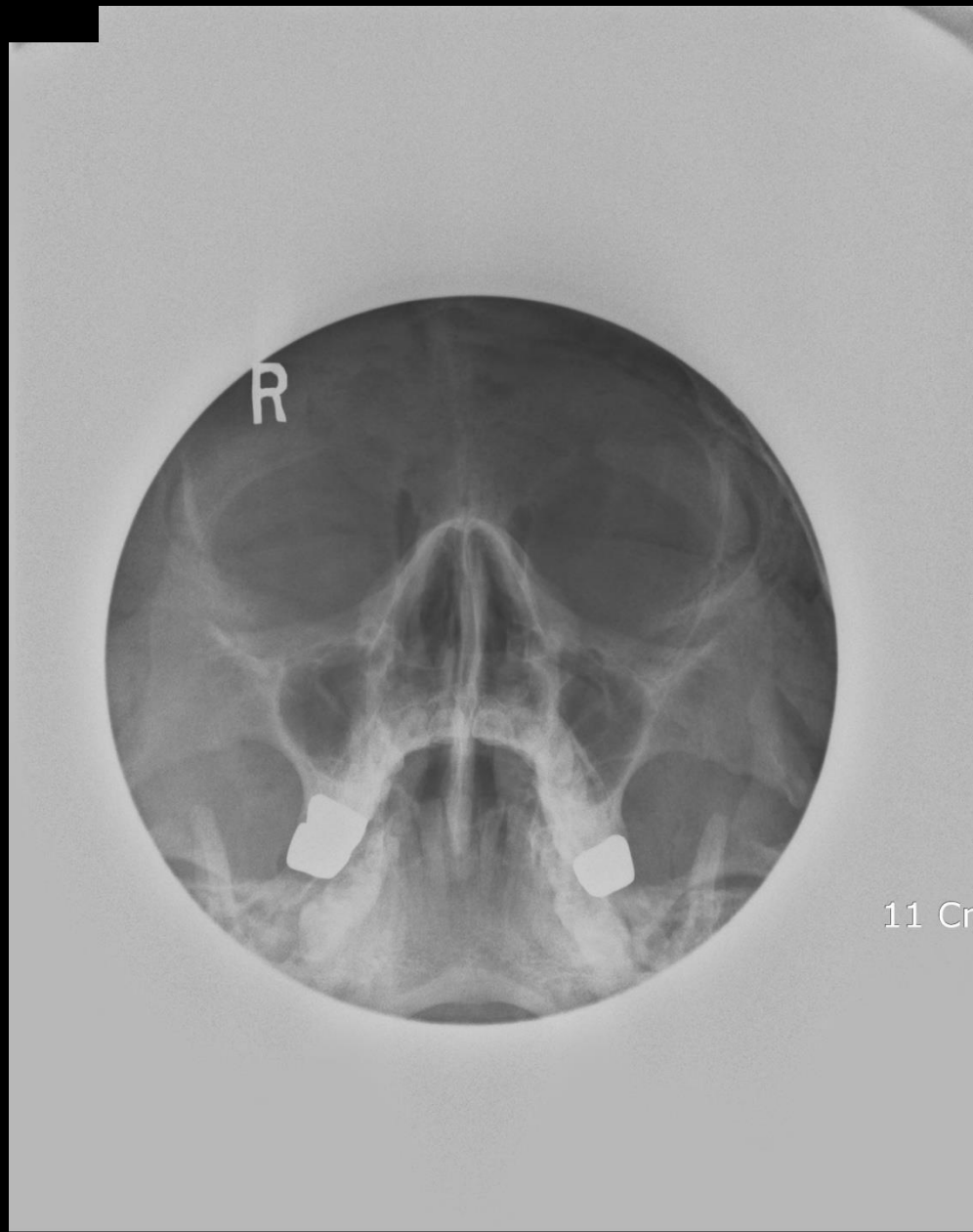
이경순



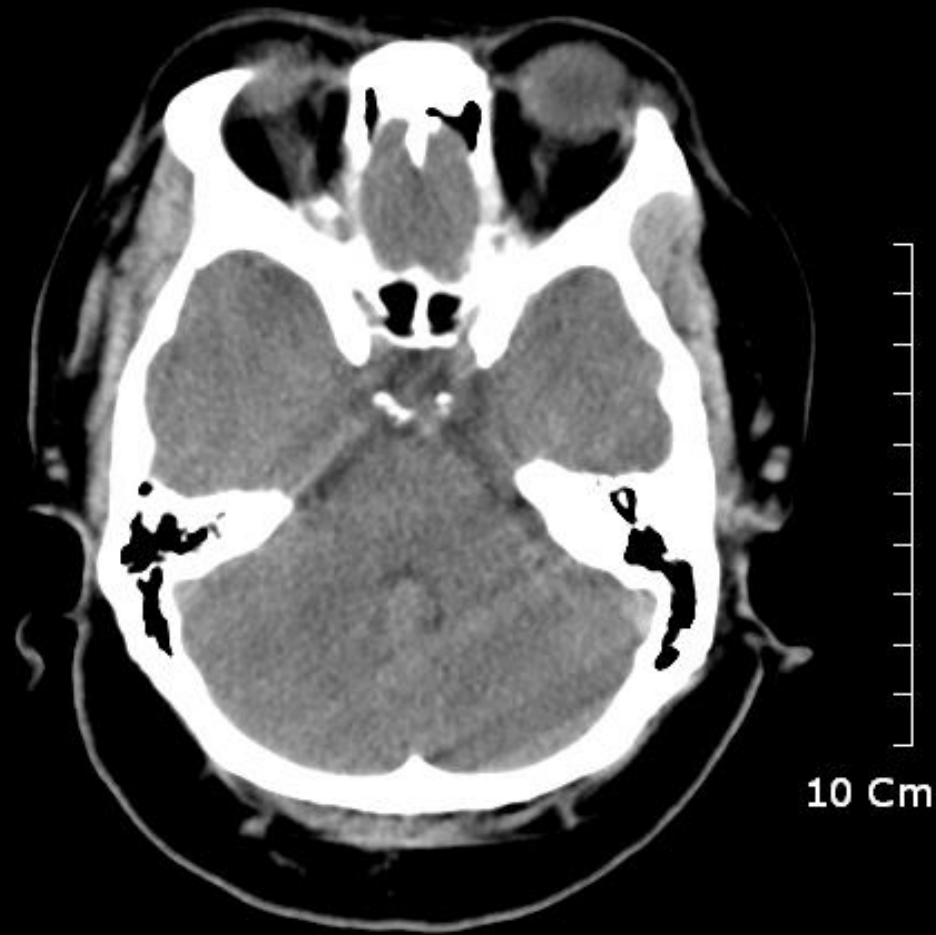
Chephalometry



PNS (Caldwell's view)



Brain CT



Abdomen sono



PFT

Severe Restrictive Lung Disease

FVC	0.67 (26%)	0.67 (26%)
FEV1	0.57 (30%)	0.61 (32%)
FEV1/FVC	85	91
DLCO, Lung Volume uncheckable		

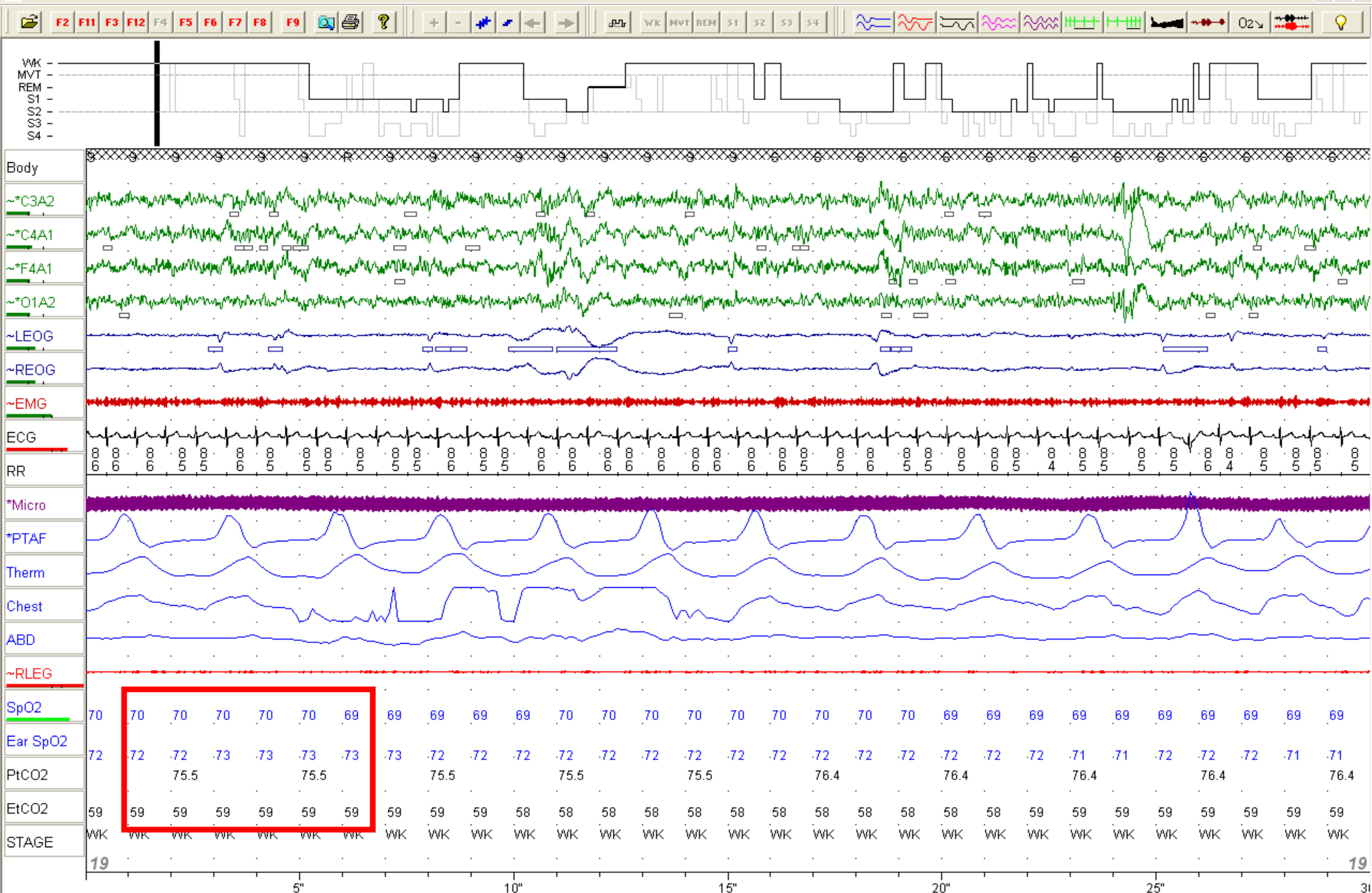
	PSG	Bi-PAP
Stage (%)	Stage N1 : 59.1% Stage N2 : 31.4% Stage N3 : 3 % Stage R : 6.6%	Stage N1 : 25.5% Stage N2 : 37.1% Stage N3 : 19.8% Stage R : 17.6%
TST	303 min	264.5 min
Arousal index(/h)	45.3	25.0



PSG data

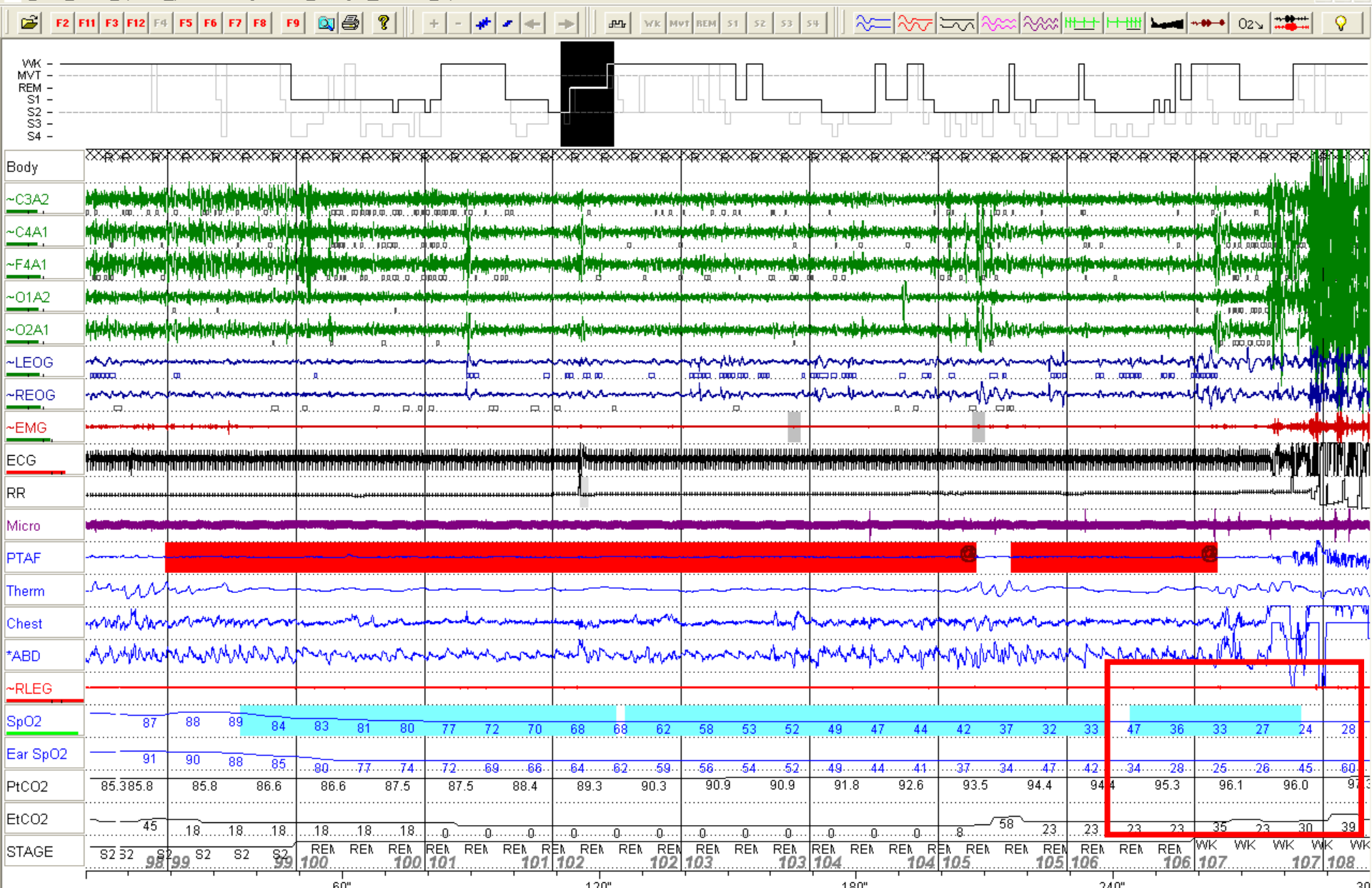
PSG ; stage W

F4 File View Report Options Multimedia Scoring Window Help



OSA (Stage R) ; O2 : 24%, CO2 : 97.3%

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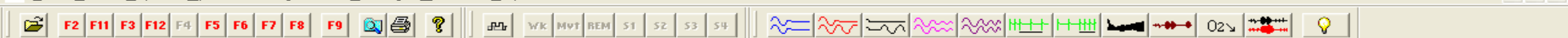




Bi-PAP data

EPAP 8 cmH2O ; CO2 99.5%

F4 File View Report Options Multimedia Scoring Window Help

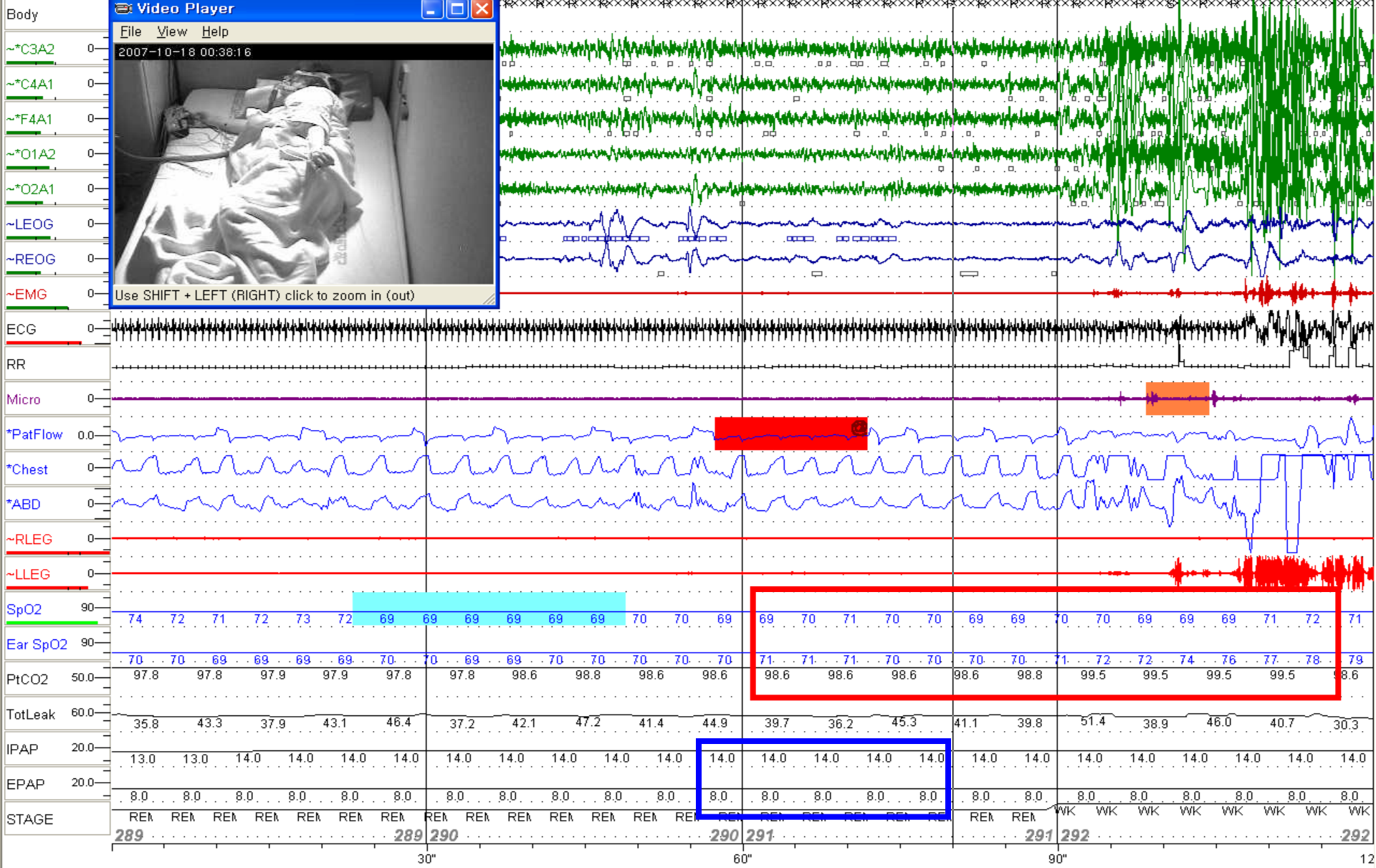


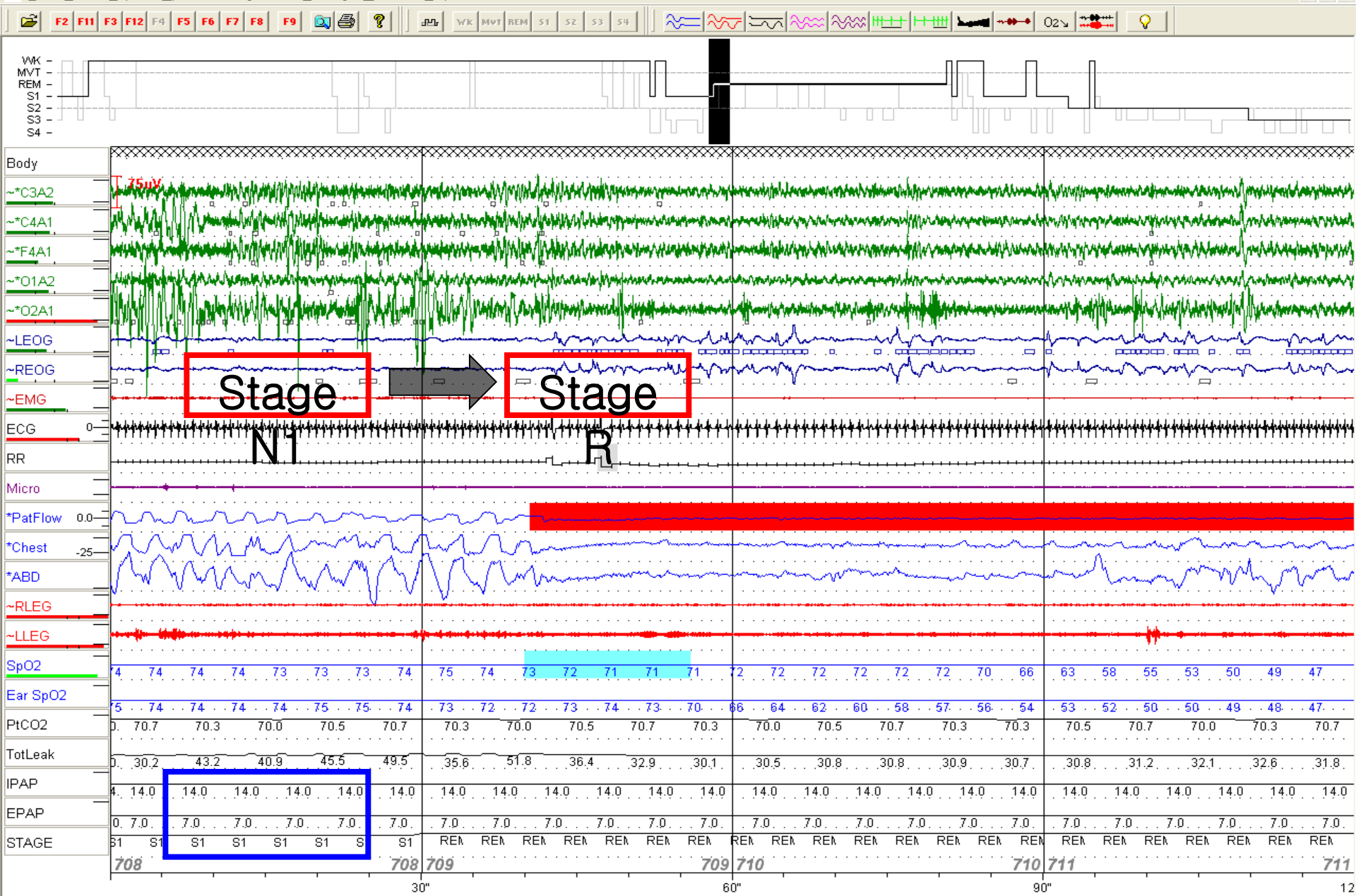
Video Player

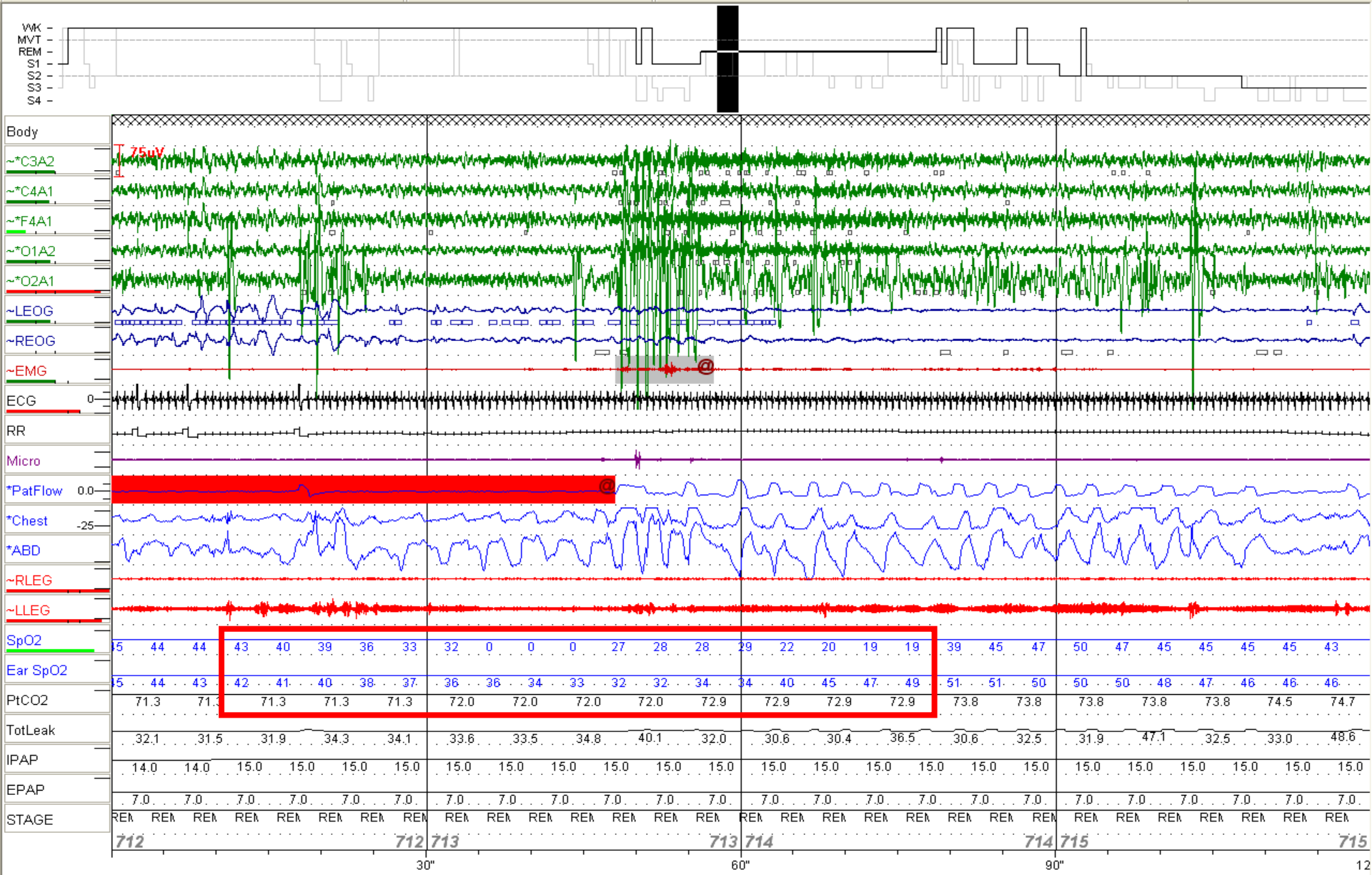
File View Help

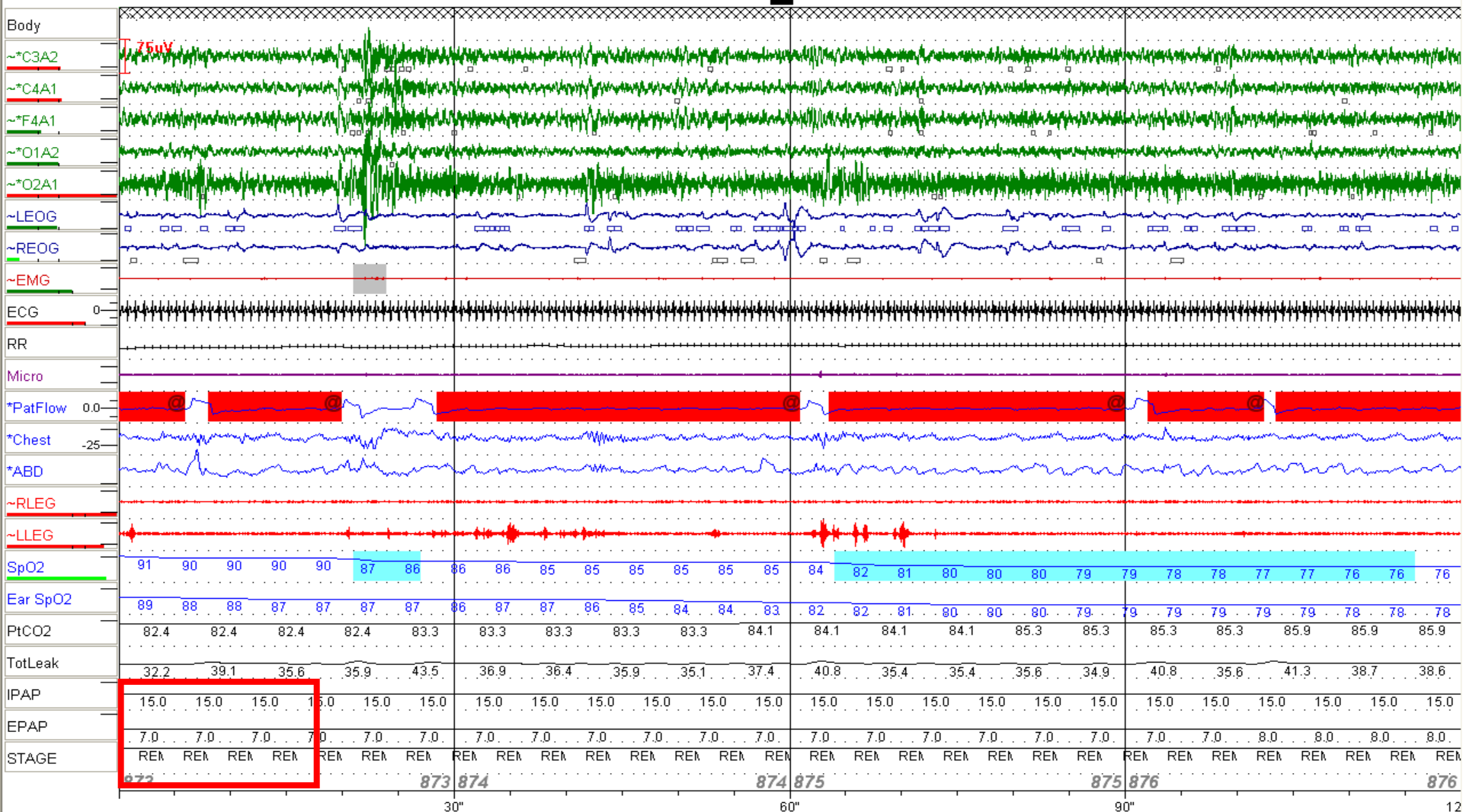
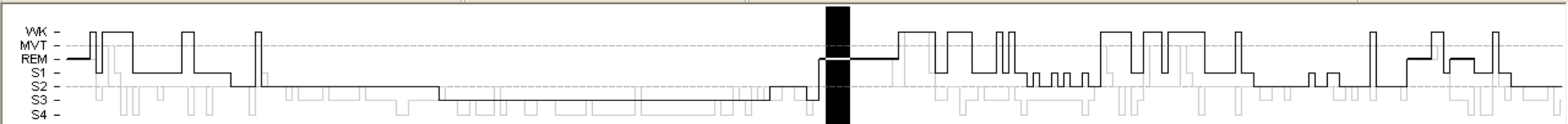
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Use SHIFT + LEFT (RIGHT) click to zoom in (out)











Diagnosis

- Obesity Hypoventilation Syndrome
- Sleep Related Hypoventilation/
Hypoxemia Due to Neuromuscular &
Chest Wall Disorders
- Restrictive lung disease
- Idiopathic right diaphragm paralysis
- Mild fatty liver

Sleep Related Hypoventilation/ Hypoxemia Due to Neuromuscular & Chest Wall Disorders

- A. A neuromuscular or chest wall disorder is present and believed to be the **primary cause** of hypoxemia.
 - B. Polysomnography or sleeping arterial blood gas determination shows **at least one of the following**;
 - i. An **SpO₂ during sleep of less than 90% for more than five minutes with a nadir of at least 85%**
 - ii. **More than 30%** of total sleep time at an SpO₂ of less than 90%
 - iii. Sleeping arterial blood gas with PaCO₂ that is **abnormally high** or **disproportionately increased** relative to levels during wakefulness
 - C. The disorder is **not better explained** by another current sleep disorder, another medical or neurological disorder, medication use, or substance use disorder.
-

Treatment

- O_2 2L via NC
- Bi-PAP (IPAP 13cmH₂O, EPAP 7cmH₂O)
- Methylphenidate

Progress

	ADM (2007.10.16)	Discharge (2007.10.22)	Follow up (2007.10.29)
Weight reduction	84.5kg	82kg	82kg
ABGA *pH	7.297	7.337	7.413
ABGA *pCO ₂	94.9 mmHg	71.7 mmHg	55.9 mmHg
ABGA *pO ₂	42.2 mmHg	63.3 mmHg	58.3 mmHg
ABGA *HCO ₃ ⁻	43.5 mmol/L	37.5 mmol/L	34.9 mmol/L
ABGA *O ₂ satu.	72.5%	90.8%	90.8%
ESS	19 (2007.10.15)	13 (2007/10/22)	6
SACS	24 (2007.10.15)	21 (2007/10/22)	19

ESS ; Epworth Sleepiness Scale, SACS ; Sleep Apnea Clinical Score

Progress

- General condition improved
- EDS ↓
- Cyanosis ↓
- Fatigue ↓
- Morning headache ↓
- Sleep in supine position without any disturbance

Admission



After Bi-PAP & O2 treatment



Admission



After Bi-PAP & O2 treatment



Diagnosis

- **History**
- **Physical examination (P/E)**
- **Blood test**
 - Arterial blood gas test**
 - Complete blood count (CBC)**
 - Electrolytes**
 - Thyroid function test (TFT)**
- **Pulmonary function test (PFT)**
- **Chest imaging study**
- **Polysomnography (PSG)**
- **Electrocardiogram (ECG)**

History & P/E

- In general, patients with OHS
 - middle-aged
 - male-to-female ratio = 2 : 1
- Classic symptoms of sleep disordered breathing (SDB)
 - fatigue, hypersomnolence, loud habitual snoring, nocturnal choking episodes, and morning headaches
- Other symptoms contrast to simple OSA
 - dyspnea, lower extremity edema
- Respiratory depressants
 - use of excessive alcohol, sedative-hypnotics, or narcotics
 - should be avoided if possible
- Obesity – BMI ≥ 30 kg/m², neck circumference, and so on
- Upper airway examination – nasal & oral cavity, pharynx, larynx

History & P/E

- **Other conditions that cause chronic hypoventilation**
 - **should be considered during the evaluation (history & P/E)**
- **Suggesting a diagnosis other than obesity hypoventilation syndrome**
 - **Mechanical limitations**
 - underlying lung disease, kyphoscoliosis, or myopathy**
 - **Neuropathic conditions**
 - diaphragmatic paralysis or neuropathy**
 - **Central control abnormalities**
 - severe hypothyroidism, cerebrovascular accident or CNS disease**

Arterial Blood Gas Test

- Arterial blood gas testing is required to confirm
 - daytime hypercapnia
 - hypoxemia
 - respiratory acidosis
- An elevated serum bicarbonate level may suggest
 - chronic hypercapnia is present
- Serum bicarbonate levels ($P < .01$)
 - OHS (hospitalized patients) – 30 ± 4 mEq/L
 - Simple obesity – 24 ± 5 mEq/L

Decision Tree to Screen

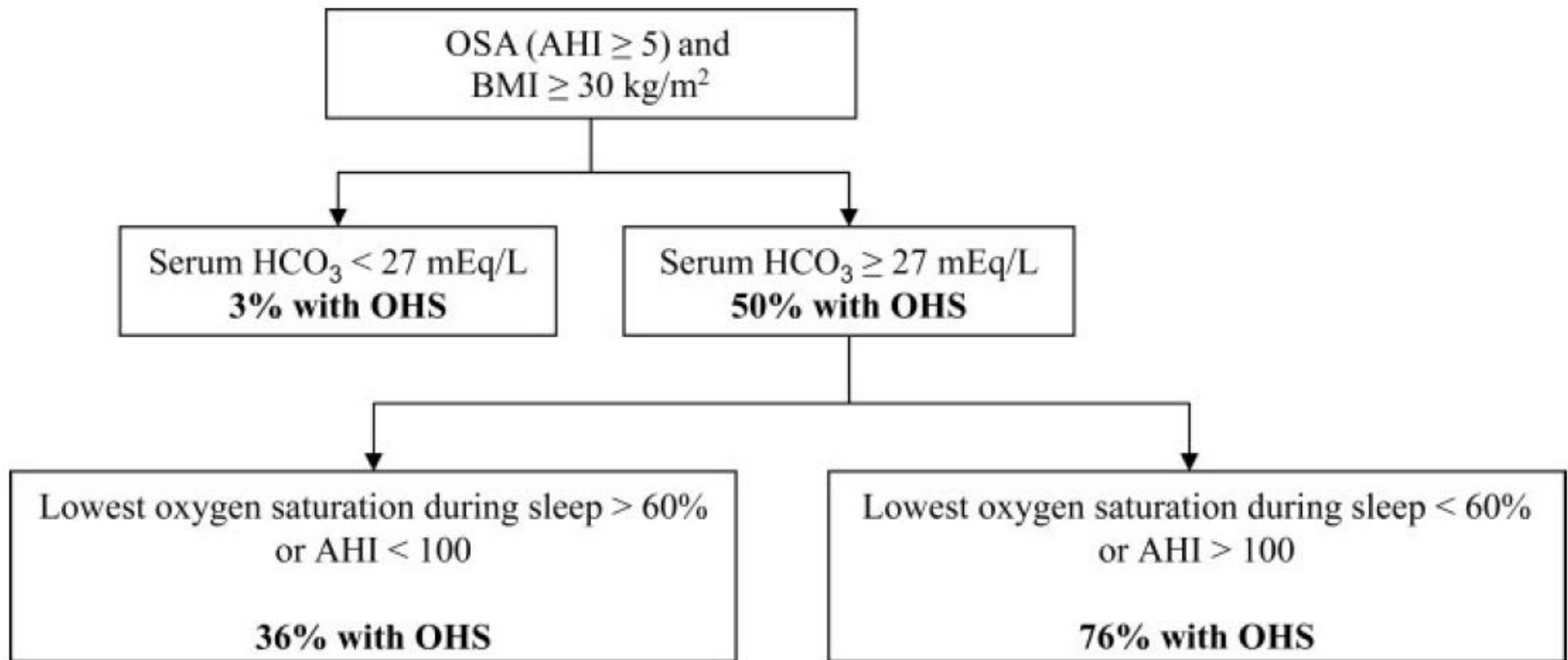


FIGURE 1. Decision tree to screen for OHS in patients with OSA (AHI ≥ 5) and BMI of ≥ 30 kg/m². The predictors were obtained from a sample of 163 patients with OSA and were validated prospectively in a sample of 359 patients with OSA.¹³

CBC & S-electrolytes

- Complete blood count (CBC)
 - to determine the existence of secondary erythrocytosis
- Serum electrolytes (including phosphorus & creatinine phosphokinase)
 - to determine additional factors that may be contributing to respiratory muscle weakness

Thyroid Function test

- **Thyroid function testing**

→ should be performed because severe hypothyroidism has been shown to cause alveolar hypoventilation in the absence of severely impaired lung function.

Glauser FL, Fairman RP, Bechard, DB. The causes and evaluation of chronic hypercapnia. *Chest*. 1987;91:755–759.
Robinson RW, Zwillich CW. Medications, sleep, and breathing. In: Kryger MH, Roth T, Dement WC, editors. Principles and practice of sleep medicine. Philadelphia, PA: W.B. Saunders Company; 2000. p.797–809.

Pulmonary Function Test

- **Pulmonary function tests**
 - should include spirometry, lung volumes, a bronchodilator response, maximal inspiratory & expiratory pressures and supine vital capacity
(if diaphragmatic paralysis is suspected)
- **Pulmonary function tests**
 - restrictive defect is common due to obesity
 - exclude to chronic obstructive pulmonary disease (COPD)
- **COPD**
 - can cause chronic hypoventilation (like OHC)
 - however, hypoventilation & hypercapnia are not common

Polysomnography

- **Night-time polysomnography testing**
 - to identify the underlying sleep disorder
 - to individualize treatment with either CPAP or NIMV
 - patients should be referred for PSG

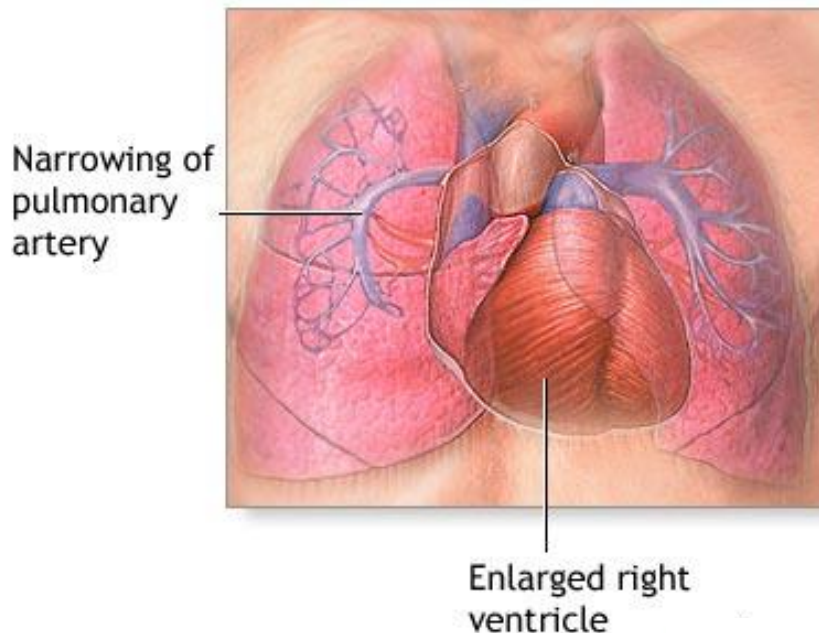
Masa JF, Celli BR, Riesco JA, et al. The obesity hypoventilation syndrome can be treated with noninvasive mechanical ventilation. *Chest*. 2001;119:1102–1107.

Koenig SM. Pulmonary complications of obesity. *Am J Med Sci*. 2001;321:249–279.

ECG

- An ECG in OHC patients could demonstrate
 - signs of right heart strain
 - right ventricular hypertrophy
 - right arterial enlargement

If left untreated → PHTN → Corpulence develop



Epidemiology

- The precise prevalence of OHS in the general population
→ remains uncertain
(because measurement of arterial blood gases is not a standard practice in patients with OSA or extreme obesity)
- The prevalence of OHS
→ ranges between 10% and 20% in pts with OSA
→ tends to be higher in men (but not as clear as in OSA)
- There is no clear racial or ethnic predominance
(the prevalence of OHS might be higher in African Americans due to
→ the high prevalence of extreme obesity → cephalometric differences)
- Because of its obesity epidemic, OHS may be
→ more prevalent in the United States than in other nations

- The prevalence is higher in the subgroup of extreme obesity (ie, BMI ≥ 40 kg/m²)

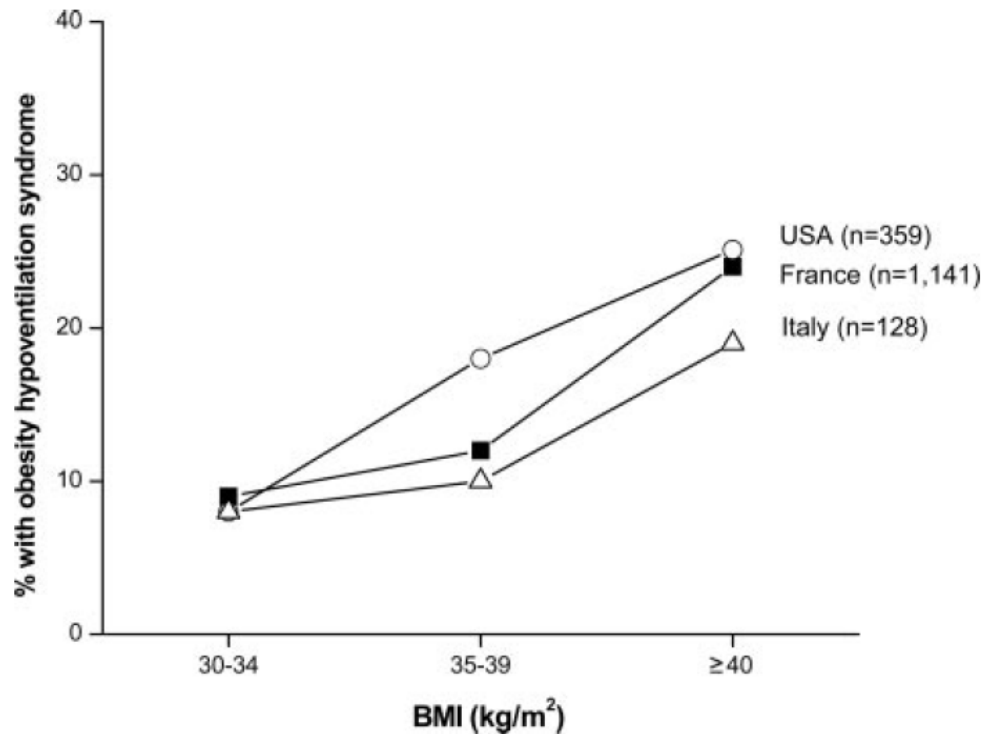


FIGURE 2. The prevalence of OHS in patients with OSA by different categories of BMI in three countries.^{13,26} The data from Italy were provided by Professor Onofrio Resta from the University of Bari, Italy.

Mokhlesi B, Tulaimat A, Faibussowitsch I, et al. Obesity hypoventilation syndrome: prevalence and predictors in patients with obstructive sleep apnea. *Sleep Breath* 2007;11:117–124

Laaban JP, Chailleux E. Daytime hypercapnia in adult patients with obstructive sleep apnea syndrome in France, before initiating nocturnal nasal continuous positive airway pressure therapy. *Chest* 2005; 127:710–715

Morbidity

- Compared to eucapnic patients with OSA, patients with OHS
 - lower quality of life
 - higher healthcare expenses
 - greater risk of pulmonary hypertension
- Mild OHS (PaCO₂ between 46 to 50 mmHg)
 - more somnolent
 - lower quality of life than patients with OSA when matched for age, BMI, and lung function
- Compared to patients with similar degrees of obesity, patients with OHS
 - increased medical resource utilization
 - more likely to be hospitalized
 - require intensive care monitoring

Hida W, Okabe S, Tatsumi K, et al. Nasal continuous positive airway pressure improves quality of life in obesity hypoventilation syndrome. *Sleep Breath* 2003; 7:3–12

Nowbar S, Burkart KM, Gonzales R, et al. Obesity-associated hypoventilation in hospitalized patients: prevalence, effects, and outcome. *Am J Med* 2004; 116:1–7

Berg G, Delaive K, Manfreda J, et al. The use of health-care resources in obesity-hypoventilation syndrome. *Chest* 2001;120:377–383

- Pulmonary hypertension is more common (50% VS 15%)
- Higher rates of ICU admission (40% VS 6%)
- Greater need for invasive mechanical ventilation (6% VS 0%)

Table 4—*Comorbidities Reported in Patients With OHS*

Conditions	Prevalence, %
Hypertension ^{12,17,28}	61–79
Heart failure ^{12,17,28}	21–32
Pulmonary hypertension (mean PAP \geq 20 mm Hg) ^{11,46}	59–88
Significant pulmonary hypertension (mean PAP \geq 40 mm Hg) ⁴⁶	31
Type 2 diabetes mellitus ^{11,17}	30–32
Asthma ^{12,17}	18–24
Erythrocytosis* ^{12,17,46}	8–15

*Hemoglobin: women, \geq 16 g/dL; men, 18 g/dL.

Mortality

- **23% OHS VS 9 % similar degree of obesity**
- **Most death : first 3months after hospital discharge**
- **OHS treated with PAP**
→ **2yr & 4yr mortality rate <10%**

■ Survival curves

→ OHS (n=47; mean BMI, 45 kg/m²)

→ Simple obesity (n=103; mean BMI, 42 kg/m²)

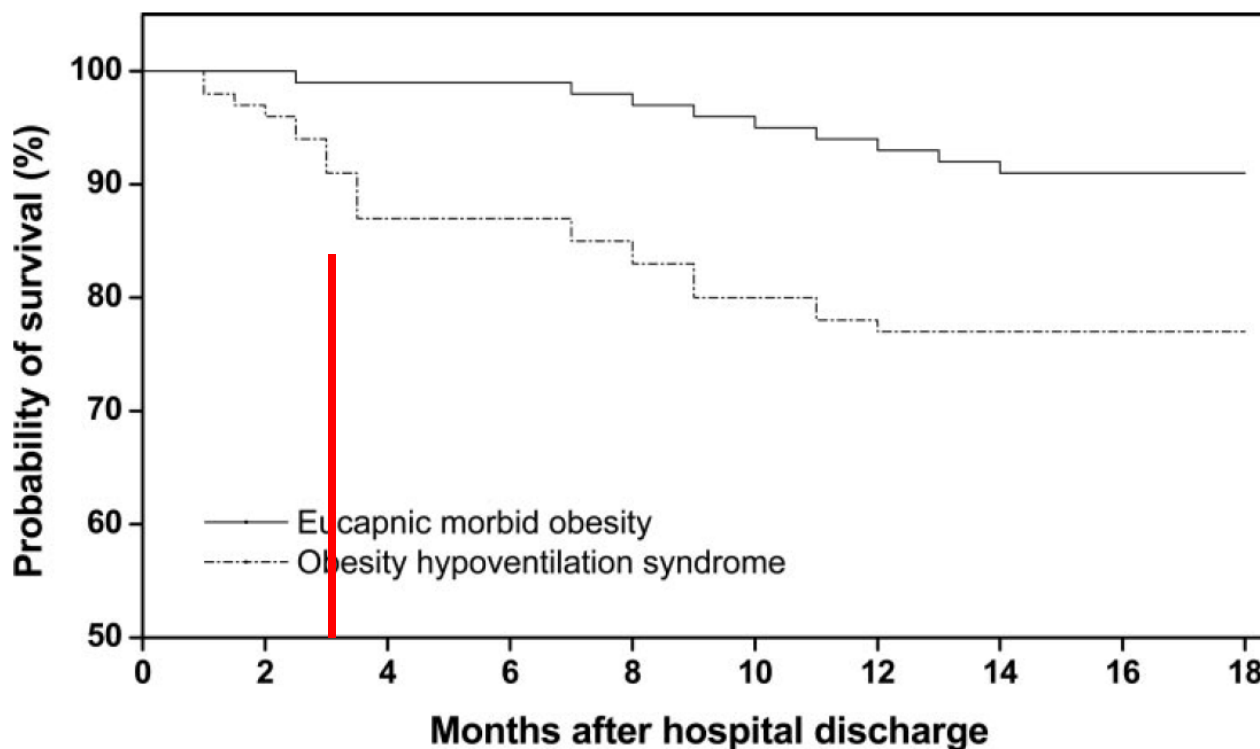


FIGURE 3. Survival curves for patients with OHS (n = 47; mean BMI, 45 kg/m²) vs simple obesity (n = 103; mean BMI, 42 kg/m²). All patients survived hospitalization, and only 13% of patients with OHS were discharged from the hospital while receiving therapy for hypoventilation. The hazards ratio for mortality in patients with OHS was 4.0 after adjustment for BMI, age, gender, electrolyte abnormalities, renal function, history of thromboembolic disease, and hypothyroidism. Reprinted from Nowbar et al²⁸ with permission from Elsevier Publishers.

Pathophysiology

- The exact mechanisms that lead to hypoventilation in obese individuals
→ remain controversial
- Since the initial description of the syndrome by Auchincloss et al in 1955
→ 3 factors have been classically tested to explain the evolution of OHC
- 3 factors
 - excessive mechanical load imposed on the resp. system by excessive wt.
 - a blunted central respiratory drive
 - sleep-disordered breathing

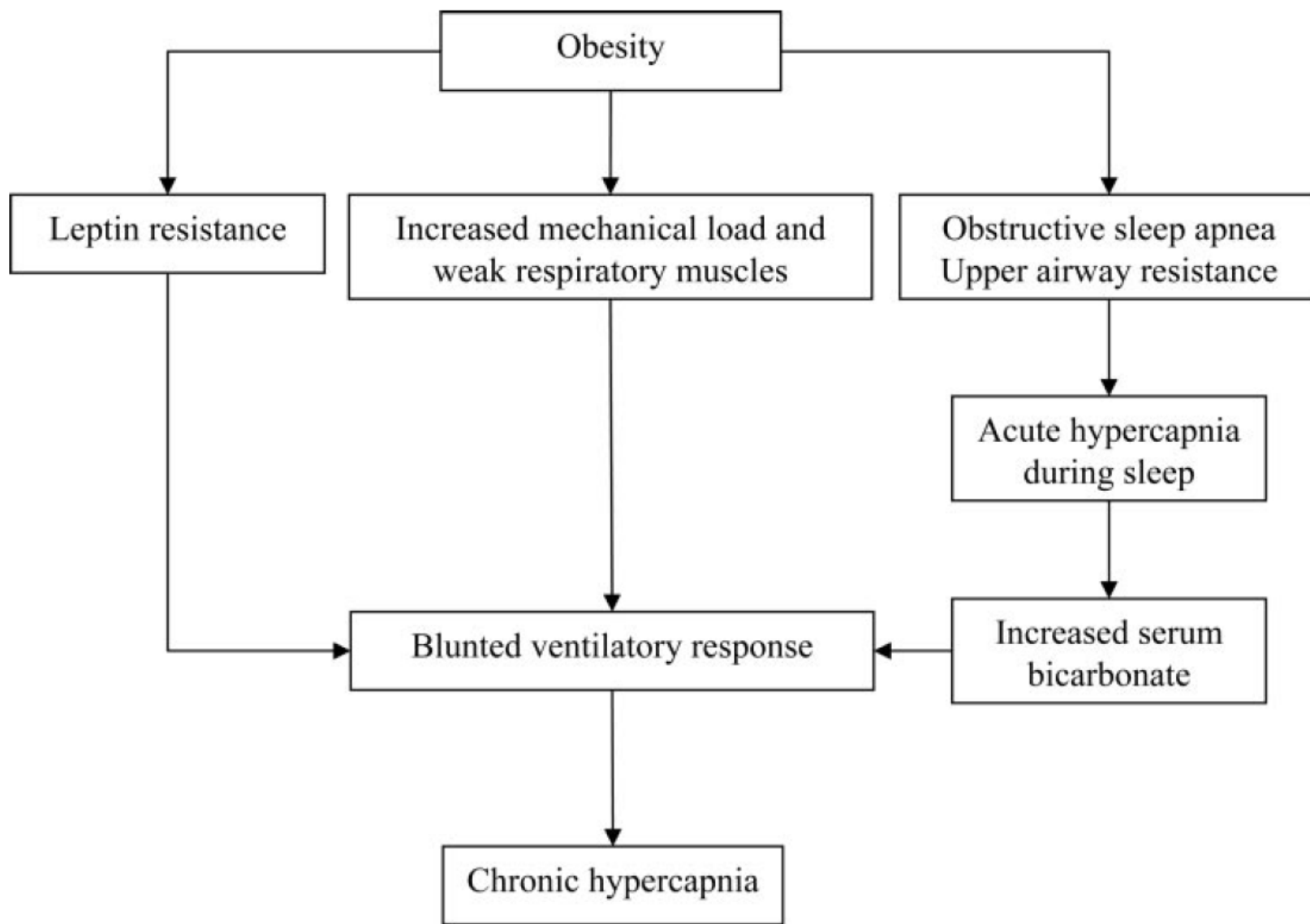


FIGURE 4. Potential mechanisms by which obesity can lead to chronic daytime hypercapnia. See the “Pathophysiology” section for a more detailed explanation.

Treatment

- **The optimal management of patients with OHS
→ remains uncertain**
- **Several studies have reported
→ improvement in chronic daytime hypercapnia & hypoxia
with PAP therapy (CPAP or bi-level PAP)**
- **Approximately half of patients with OHS require
→ oxygen therapy in addition to PAP therapy upon initiation of
treatment**
- **Although PAP is the mainstay of therapy in both OSA and
OHS patients,
→ there is no standard protocol for its titration**

PAP therapy

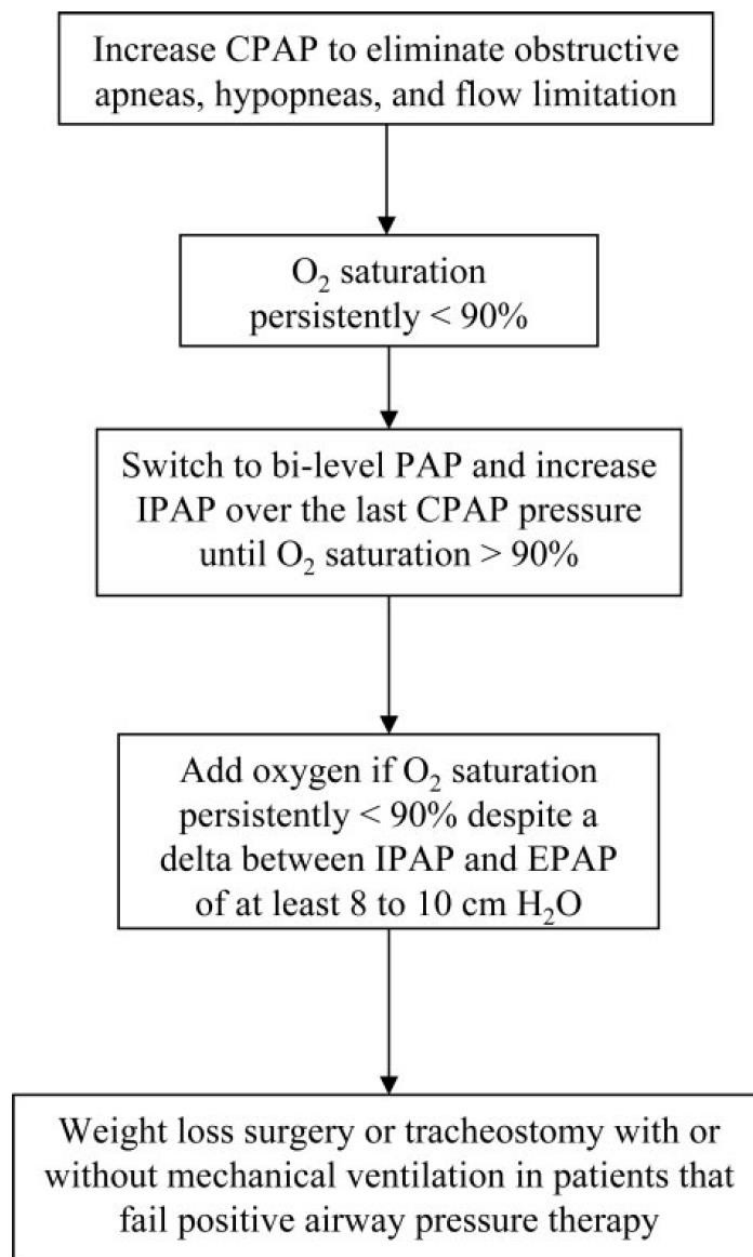


FIGURE 5. Therapeutic algorithm during PAP titration in patients with OHS. See “PAP Therapy” section for a more detailed explanation.

Berger KI, Ayappa I, Chatr-Amontri B, et al. Obesity hypoventilation syndrome as a spectrum of respiratory disturbances during sleep. *Chest* 2001; 120:1231–1238

Mokhlesi B, Tulaimat A. Recent advances in obesity hypoventilation syndrome. *Chest*. 2007 Oct;132(4):1322-36.

Treatment

- Weight reduction surgery

- Bariatric surgery

- ; drop in BMI 56 kg/m² → 36 kg/m²

- AHI 72 → 19

- Verse T. Bariatric surgery for obstructive sleep apnea.*

- Chest 2005; 128:485-487*

- Tracheostomy

- retrospective study of 13 patient with OHS
significant improvement in OSA

- J Gastrointest Surg 2002; 6:354-358*

- no large studies evaluating long-term outcome

Treatment

- Medroxyprogesterone

- respiratory response at the hypothalamus through an estrogen-dependent progesterone receptor

- In a series of **10 patient** ; treatment

PaCO₂ ; **51** → **38** mmHg

PaO₂ ; **49** → **62** mmHg

Ann Intern Med 1975; 83:476-479

- Acetazolamide

- carbonic anhydrase inhibitor

- cause **metabolic acidosis**

- **Increase minute ventilation & reduces PaCO₂**

Conclusion

- With such a global epidemic of obesity
→ the prevalence of OHS is likely to increase
- Despite the significant morbidity & mortality associated with OHS
→ it is often unrecognized and treatment is frequently delayed
- **Further research** is needed
→ to better **understand the pathophysiology** & **long-term treatment outcomes** of patients with OHS



Thank you for your attention!

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