



Ελληνική Πνευμονολογική Εταιρεία



26^ο Πανελλήνιο

ΠΝΕΥΜΟΝΟΛΟΓΙΚΟ ΣΥΝΕΔΡΙΟ

9-12 Νοεμβρίου 2017

Athens Hilton Hotel, Αθήνα

ΧΑΠ και σύνδρομο υπνικής άπνοιας



Πασχάλης Στειρόπουλος
Επίκουρος Καθηγητής Πνευμονολογίας
Τμήμα Ιατρικής ΔΠΘ

Δήλωση σύγκρουσης συμφερόντων



- Participated in advisory boards of the following companies: AstraZeneca, Boehringer-Ingelheim, Chiesi, Elpen, Menarini, Novartis
- Received honoraria και travel grants from the following companies: AstraZeneca, Boehringer-Ingelheim, Chiesi, Elpen, Menarini, Novartis, Teva



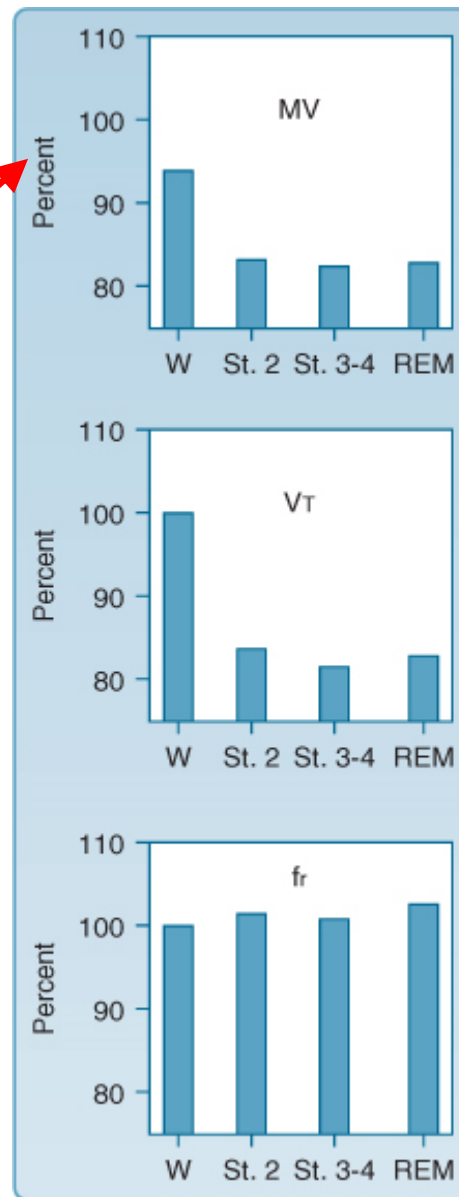
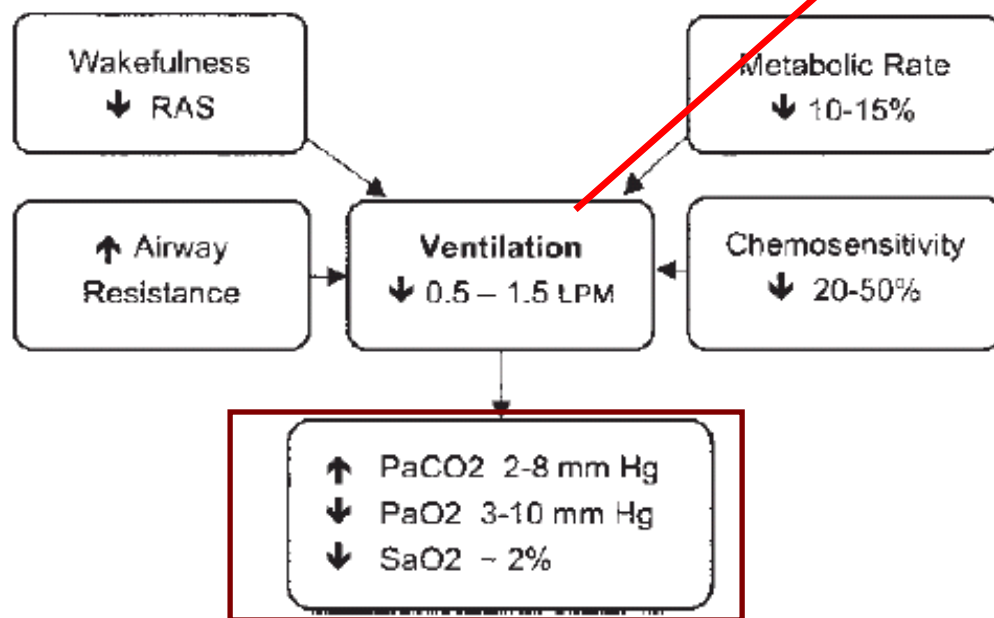
Δομή

A. Εισαγωγή

- Επίδραση του ύπνου στην αναπνοή
- Επίδραση της ΧΑΠ στον ύπνο
- Διαταραχές του ύπνου στους ασθενείς με ΧΑΠ

B. ΧΑΠ και ΣΑΥ (Overlap syndrome)

Επίδραση του ύπνου στην αναπνοή

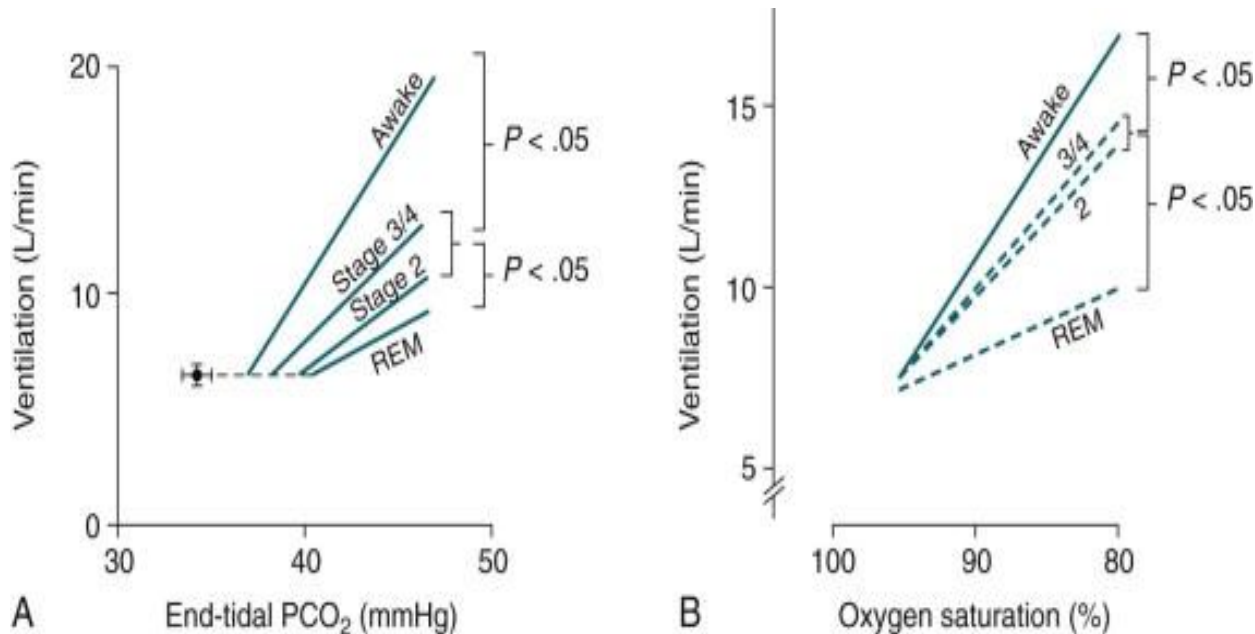


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Επίδραση του ύπνου στην αναπνοή



- **A** The hypercapnic ventilatory response is reduced during NREM sleep compared with wake and decreased in REM sleep compared with NREM sleep
- **B** The hypoxic ventilatory response is also decreased during REM compared with wake and REM compared with NREM



Douglas NJ, White DP, Weil JV, et al. Hypercapnic ventilatory response in sleeping adults. Am Rev Respir Dis 1982;126:286–289

Effects of COPD on Sleep



Cough and wheezing interrupt and delay sleep

Klink M. Chest 1987

Sleep is more fragmented, with increased arousals and reduced amounts of deep nREM and REM sleep

McSharry DG, Respiriology 2012

Severity of COPD correlates with severity of subjective sleep complaints, but not with objectively measured sleep variables

Omachi TI Sleep Med 2012

Hynninen MJ Sleep Med 2013

Effects of COPD on Sleep



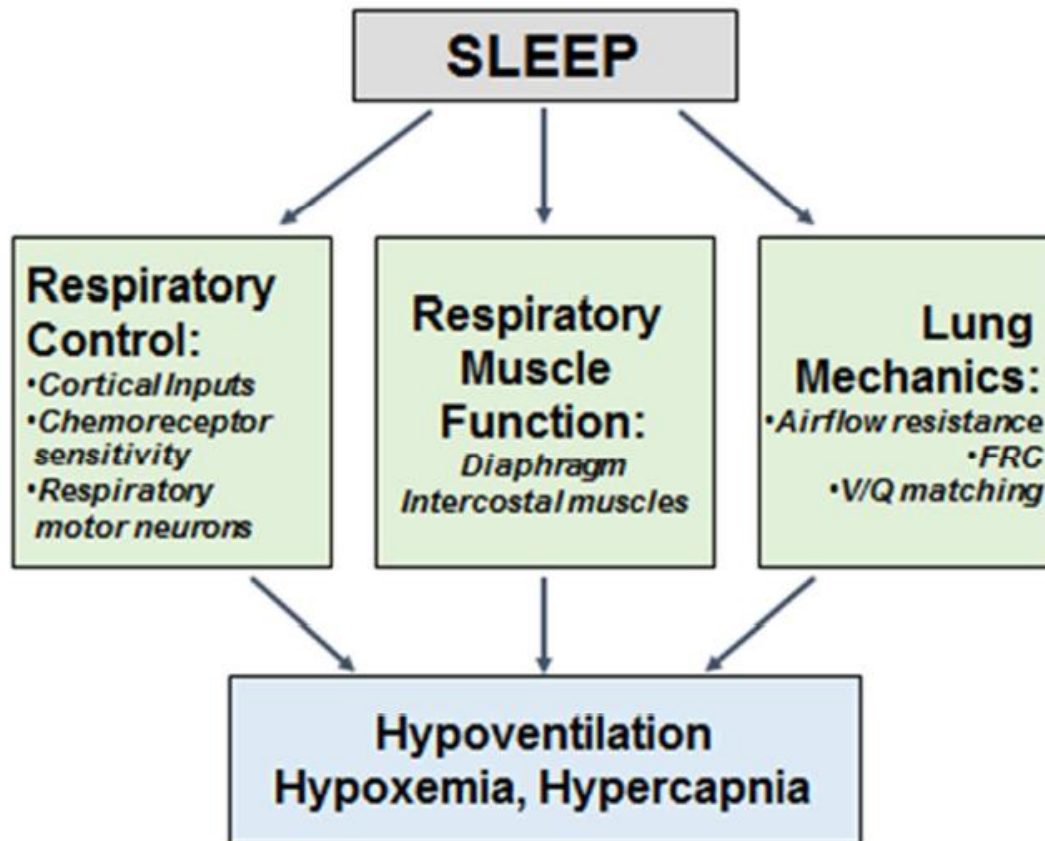
- Daytime sleepiness (by Epworth) and poor quality sleep (by PSQI) compared to that of matched controls

Zohal A Glob J Health Sci 2013

- Increased prevalence of insomnia complaints
- Increased use of hypnotics

McNicholas WT Sleep Breath 2013

Επίδραση του ύπνου στην αναπνοή



Effects of Sleep on Patients with COPD



- Patients with COPD are most profoundly hypoxemic at night

McNicholas WT, Chest 2000

- COPD patients are more likely to die at night

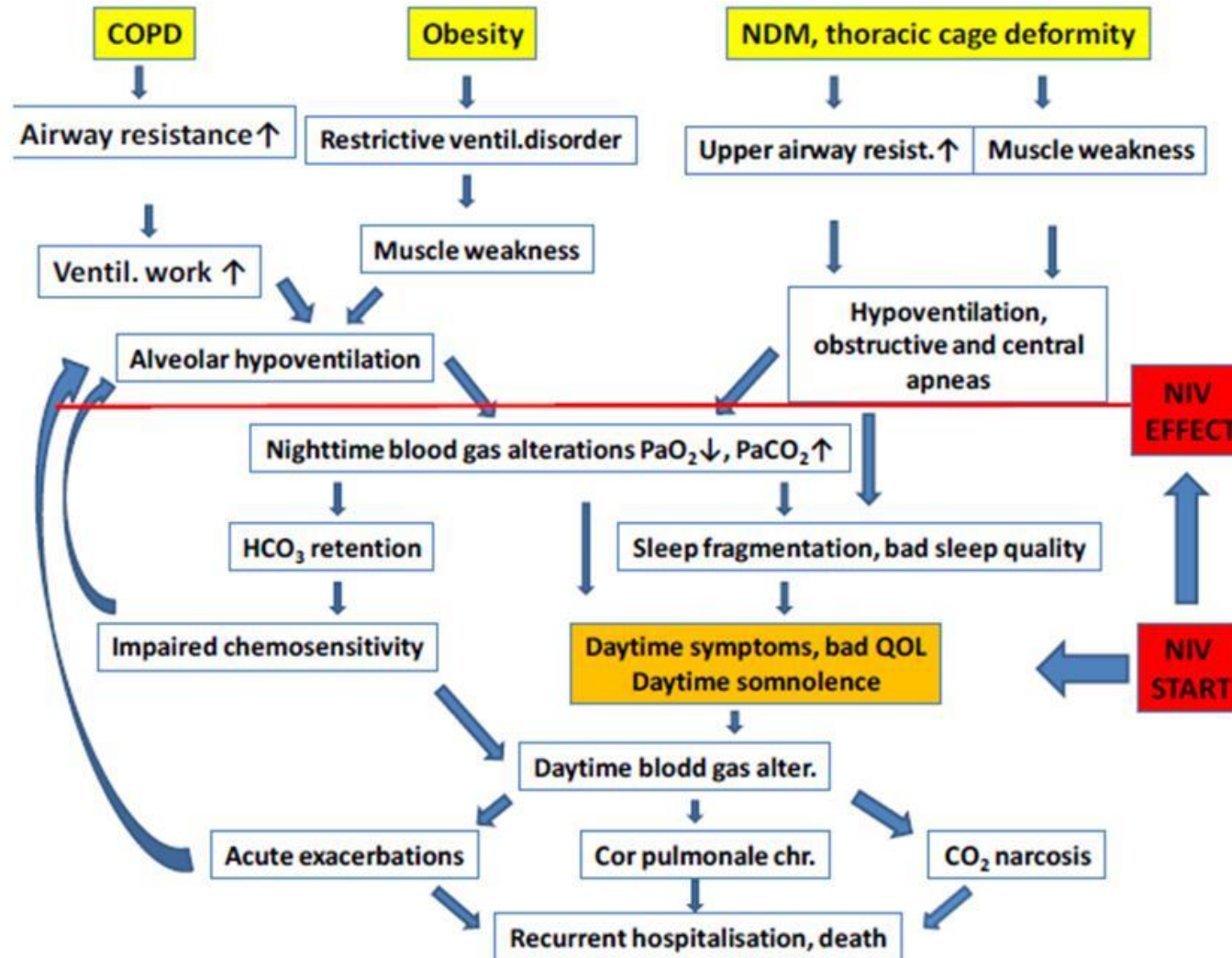
McNicholas WT Br Med J 1984

- Oxygen desaturation is greater during sleep than during exercise in COPD, and wake SaO_2 predicts nocturnal desaturation better than exercise SaO_2 or wake PaCO_2

Mulloy E, Chest 1996



HYPOVENTILATION SYNDROMES



COPD and Poor Sleep: A Two Way Street



- How does sleep impact COPD?
 - Reduced chemosensitivity
 - Reduced pulmonary function
 - Impaired muscle performance
 - Systemic inflammation
- How does COPD impact sleep?
 - Symptoms cause sleep disturbance
 - Hypoxemia and hypercarbia disturb sleep

ΧΑΠ και ύπνος



Original Article

Disturbed sleep among COPD patients is longitudinally associated with mortality and adverse COPD outcomes

Theodore A. Omachi ^{a,*}, Paul D. Blanc ^b, David M. Claman ^a, Hubert Chen ^a, Edward H. Yelin ^{c,d},
Laura Julian ^d, Patricia P. Katz ^{c,d}

Sleep Medicine 13 (2012) 476–483

Cross-sectional association of disturbed sleep with COPD symptoms and severity among 98 COPD subjects.

	OR (95% CI)	p-Value
Cough symptoms	3.3 (1.1–9.7)	0.034
Dyspnea Scale ^a	1.4 (1.1–1.7)	0.004
COPD Severity Score ^b	1.9 (1.1–3.2)	0.015
Oxygen saturation ≤92%	2.2 (0.7–6.5)	0.18
FEV ₁ ^c	0.97 (0.4–2.2)	0.94

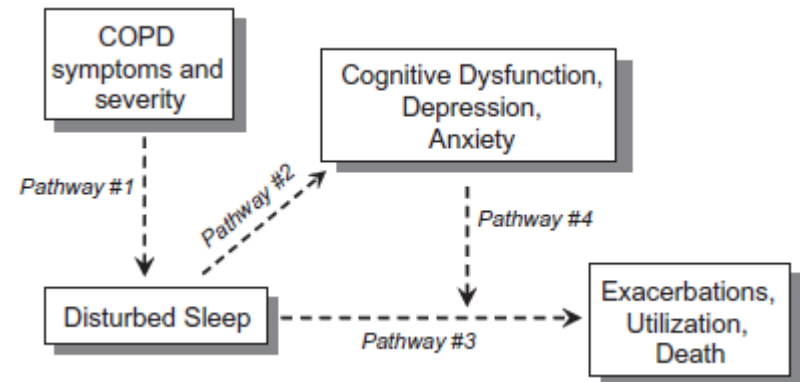


Table 6
Secondary analysis: Association between sleep disturbance at baseline and subsequent health outcomes, by COPD GOLD stage.

	COPD exacerbations OR (95% CI) p-value	Respiratory-related emergency utilization OR (95% CI) p-value	All-cause mortality HR (95% CI) p-value
GOLD 1 and 2 (n = 56)	1.9 (0.5–7.4) p = 0.38	3.9 (0.5–33) p = 0.21	3.2 (0.2–50) p = 0.42
GOLD 3 and 4 (n = 42)	N/A ^a	15.1 (1.4–159) p = 0.02	4.5 (1.3–16) p = 0.02

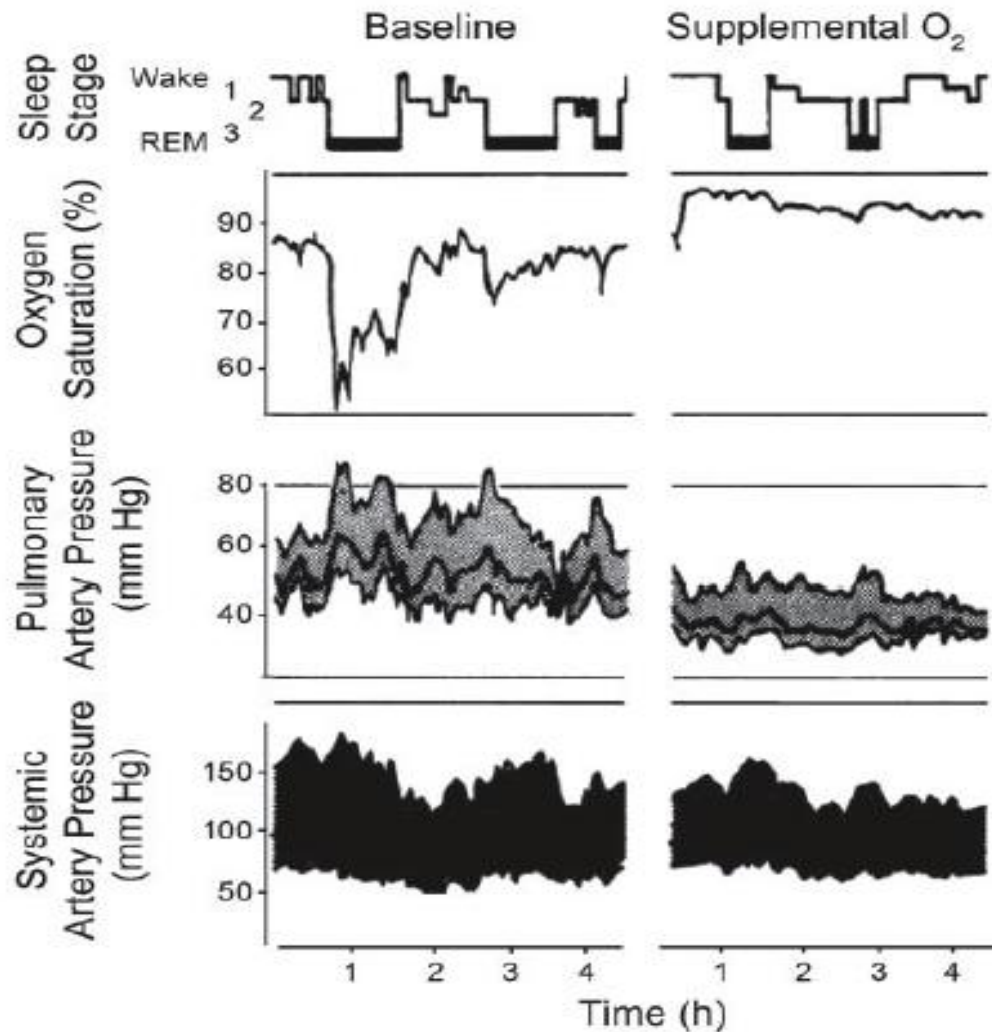
Pulmonary Rehabilitation improves sleep in COPD



- Exercise is known to promote and to consolidate sleep
- In this study of 64 patients with severe COPD (FEV_1 53%), 8 weeks of pulmonary rehab improved Pittsburgh Sleep Quality Index (PSQI) and Health-related Quality of Life (HRQoL).

Soler X, COPD 2013

Effect of nocturnal nasal oxygen on SaO_2 , systemic and pulmonary artery pressures





Sleep Disorders in Chronic Obstructive Pulmonary Disease: Etiology, Impact, and Management

Rohit Budhiraja, MD¹; Tauseef A. Siddiqi, MD²; Stuart F. Quan, MD^{2,3}

¹Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Medicine, Tufts Medical Center, Boston, MA;

²Division of Allergy, Critical Care, Pulmonary and Sleep Medicine, Department of Medicine, University of Arizona College of Medicine, Tucson, AZ; ³Divisions of Sleep Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

Journal of Clinical Sleep Medicine, Vol. 11, No. 3, 2015

1. Αϋπνία
2. Νυχτερινή υποξυγοναιμία
3. Νυχτερινός υποαερισμός
4. Σύνδρομο ανήσυχων άκρων
5. ΣΑΥ



OSA + COPD= Overlap Syndrome

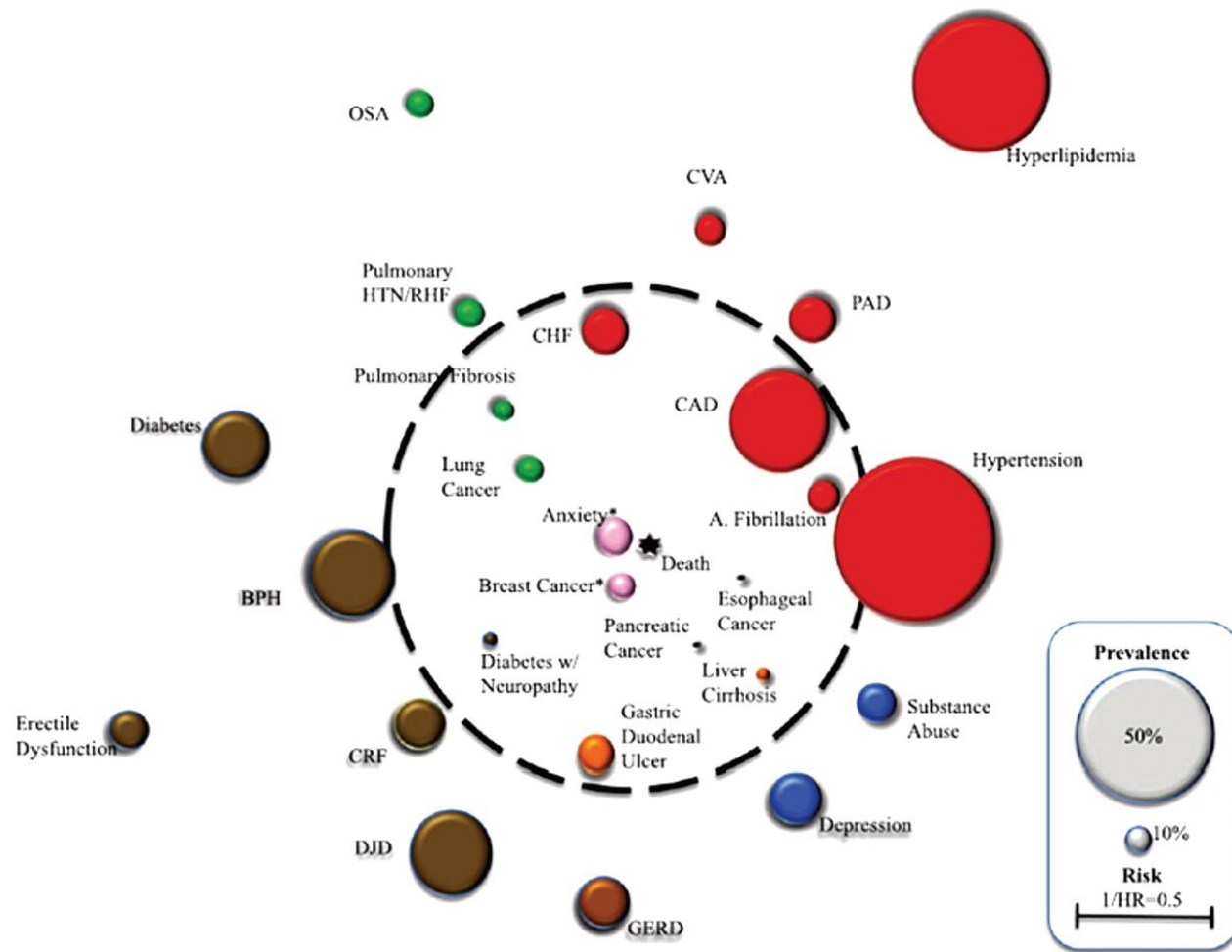
Η ΧΑΠ και το ΣΑΥ είναι παθολογικές καταστάσεις που χαρακτηρίζονται από υψηλό επιπολασμό, που υπολογίζεται στο 10%, αν και η συχνότητα των διαταραχών της αναπνοής στον ύπνο (sleep-disordered breathing- SDB) είναι σημαντικά υψηλότερη

Diaz Guzman E. Clin Chest Med 2014

Senaratna CV et al Sleep Med Rev 2016

Heinzer R et al. Lancet Respir Med 2015

Η ταυτόχρονη παρουσία τους αποτελεί την κλινική οντότητα που ονομάζεται **Σύνδρομο Επικάλυψης (Overlap Syndrome)**



Σύνδρομο αλληλοεπικάλυψης ΧΑΠ-ΣΑΥ (overlap syndrome)



Η συνύπαρξη και των δυο νοσημάτων (ΧΑΠ και ΣΑΥ) ταυτόχρονα σε έναν ασθενή αποτελεί το σύνδρομο αλληλοεπικάλυψης όπως περιγράφηκε για πρώτη φορά από τον David Flenley το 1985

Ο επιπολασμός του συνδρόμου στο γενικό πληθυσμό από εκτιμήσεις ταυτόχρονα και των δυο παθήσεων είναι 1% αλλά αναμένεται να αυξηθεί λόγω και της αυξανόμενης επίπτωσης της παχυσαρκίας, ως παράγοντα κινδύνου, στο γενικό πληθυσμό

McNicholas WT. Chronic obstructive pulmonary disease and obstructive sleep apnoea-the overlap syndrome. J Thorac Dis 2016;8:236–242

Σε μία πρόσφατη μελέτη παρατήρησης διαπιστώθηκε ότι το ΣΑΥ είναι ιδιαίτερο συχνό σε ασθενείς με σοβαρού βαθμού ΧΑΠ αναδεικνύοντας τη συσχέτιση μεταξύ του ΣΑΥ και της σοβαρότητας της απόφραξης

Soler X, 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

OSA + COPD=Overlap Syndrome



- **Definitions of COPD and OSA vary, so....prevalence estimates of the overlap syndrome vary**
- As many as 15% of COPD patients have co-existent OSA
Carratu P ERJ 2008
- In patients with OSA, prevalence of COPD is 7.6% (compared to patients without OSA, where prevalence is 3.7%)
Greenberg-Dotan S, Sleep Breath 2013
- For patients with GOLD stage 4 COPD, the prevalence of OSA is 43%
Areias V, Rev Port Pneumol 2014

Σύνδρομο αλληλοεπικάλυψης ΧΑΠ-ΣΑΥ (overlap syndrome)



Ωστόσο, σε προγενέστερες πολυκεντρικές μελέτες που αφορούσαν στην εκτίμηση καρδιαγγειακών παραγόντων (Sleep Heart Health Study and Multinational Monitoring of Trends and Determinants in Cardiovascular Disease-MONICA II) δε βρέθηκε συσχέτιση μεταξύ των δυο παθήσεων

Οι δυο αυτές μελέτες είχαν ένα βασικό περιορισμό, τη χρήση ασθενών με ήπιο βαθμό απόφραξης, γεγονός που επιβεβαιώνει τα νεότερα δεδομένα, ότι δηλαδή ασθενείς με σοβαρού βαθμού ΧΑΠ παρουσιάζουν αυξημένο κίνδυνο να έχουν και ΣΑΥ

Αξιοσημείωτο είναι ότι, από τις δύο προαναφερθείσες μελέτες (Sleep Heart Health Study και MONICA II), οι ασθενείς με GOLD II στάδιο ΧΑΠ ήταν 19% και 11% αντιστοίχως, ενώ οι ασθενείς με ΣΑΥ ήταν 14% και 11% αντίστοιχα

Current evidence on prevalence and clinical outcomes of co-morbid obstructive sleep apnea and chronic obstructive pulmonary disease: A systematic review



Md Shajedur R. Shawon ^a, Jennifer L. Perret ^{c, d}, Chamara V. Senaratna ^{c, e}, Caroline Lodge ^c, Garun S. Hamilton ^{b, 1, *}, Shyamali C. Dharmage ^{c, 1}

Sleep Medicine Reviews 32 (2017) 58–68

Table 1

Prevalence of overlap syndrome in general and hospital population.

Authors, year, reference	Country	Sampling	Characteristics of study participants	COPD Dx/OSA Dx	AHI cut off per hour	Oxygen desaturation for hypopnea	Prevalence of COPD	Prevalence of OSA	Prevalence of overlap syndrome
General population									
Azuma et al., 2014 [20]	Japan	Sample taken from an urban wholesale company (n = 303)	Mean age 43.9 ± 8.2 and all male	Spirometry/actigraph	AHI ≥ 5	>3%	6.3%	59.7%	3.6%
Bednarek et al., 2005 [18]	Poland	Random population sample (n = 676)	Age range was 41–72 y and 52% male	Spirometry/lab PSG	AHI > 5	≥2%	10%	11.7%	1%
Sanders et al., 2003 [19]	USA	Random sample from sleep heart health study (n = 5954)	>40 y were included and mean age of 63 y; 47% male	Spirometry/unattended home PSG	AHI > 15	≥4%	19.1%	18%	2.7%
Hospital population									
Ganga et al., 2013 [21]	USA	Consecutive elderly (≥65 y) in-patients (n = 2873)	Age range was 65–89 y	Treatment/sleep laboratory	AHI > 5	≥3%	15.5%	3%	1%
Stanchina et al., 2013 [22]	USA	Consecutive patients from outpatient department (n = 10,721)	Mean age of OSA = 61.6; COPD = 69 and overlap syndrome = 61.4 y	CPT codes			10.4%	21.3%	2.1%



Current evidence on prevalence and clinical outcomes of co-morbid obstructive sleep apnea and chronic obstructive pulmonary disease: A systematic review

Md Shajedur R. Shawon^a, Jennifer L. Perret^{c, d}, Chamara V. Senaratna^{c, e}, Caroline Lodge^c, Garun S. Hamilton^{b, 1, *}, Shyamali C. Dharmage^{c, 1}

Sleep Medicine Reviews 32 (2017) 58–68

Table 2
Prevalence of overlap syndrome among OSA patient groups.

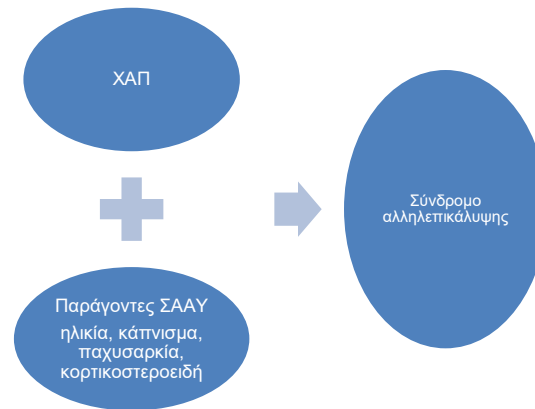
Authors, year, reference	Country	Sampling	Characteristics of study participants	COPD Dx/OSA Dx	AHI cut off per hour	Oxygen desaturation for hypopnea	Prevalence of overlap syndrome	Remarks
Chaouat et al., 1995 [7]	France	Consecutively recruited sleep lab patients (n = 265)	Mean age 54 ± 10 y and 92% male	Spirometry/lab PSG	AHI > 20		11%	Older OS group (p = 0.01)
Chokhani et al., 2005 [25]	Nepal	Consecutively recruited sleep patients excluding those with an AHI < 5 (n = 89)	Mean age (OSA) 57 y (range 6–85); 69.6% male	COPD medication/home PSG	AHI > 5	≥4%	43.8%	
Greenberg-Dotan et al., 2014 [34]	Israel	Consecutively recruited 1497 adult OSA patients	Mean age 55.5 ± 11.1 y; 76.5% male	ICD9 code/lab PSG	AHI > 5	≥4%	7.6%	
Lopez et al., 2009 [23]	Puerto Rico	Consecutively recruited sleep lab patients (n = 52)		Spirometry/lab PSG	AHI > 5 with symptoms or AHI > 15 without symptoms		55.7%	
O'Brien et al., 2005 [24]	Ireland	Consecutive patients with OSA with CPAP therapy (n = 120)		Physician/home PSG	AHI > 5 with symptoms or AHI > 10 without symptoms	≥3%	41%	Older OS group (p = 0.008)
Rizzi et al., 1997 [33]	Italy	Consecutively recruited sleep lab patients (n = 168)	Mean age 56 ± 10 y and 86% male	Spirometry/lab PSG	AHI > 15	≥4%	19.5%	
Shiina et al., 2012 [26]	Japan	Consecutively recruited sleep lab patients (n = 524)	Mean age of 50.4 y and all male	Spirometry/lab PSG	AHI ≥ 5	≥3%	12%	Older OS group (p < 0.01)



Prevalence of overlap syndrome among COPD patient groups.

Authors, year, reference	Country	Sampling	Characteristics of study participants	COPD Dx/OSA Dx	AHI cut off per hour	Oxygen desaturation for hypopnea	Prevalence of overlap syndrome
Diomidous et al., 2012 [27]	Greece	Elderly COPD patients (≥ 70 y) purposively selected (n = 500)	55% male	Spirometry/ESS and Berlin questionnaires			21.4%
Kumar et al., 2013 [28]	India	Consecutive patients with confirmed COPD from outpatient clinic (n = 72)		Spirometry/ESS & Berlin questionnaires			18.0%
Larsson et al., 2001 [38]	Sweden	Bronchitic patients were selected from a population study (n = 471)		Treatment/home PSG	AHI ≥ 10 plus daytime symptoms	$\geq 4\%$	5.4%
Machado et al., 2010 [29]	Brazil	Consecutively recruited hypoxemic COPD patients receiving LTOT (n = 603)		Spirometry/lab PSG	AHI > 15	$\geq 3\%$	15.7%
Perimenis et al., 2007 [43]	Greece	Consecutive COPD patients from outpatient Clinic (n = 720)	All male patients	Spirometry/lab PSG	AHI > 5 with symptoms	>2%	10.28%
Shaya et al., 2009 [15]	USA	A COPD cohort from Medicaid insurance beneficiaries (n = 3455)	Mean age 52.4 y	ICD9 codes/ICD9 codes			2.87%
Soler et al., 2015 [30]	USA	Consecutive patients aged >40 y with confirmed diagnosis of COPD (Moderate to severe cases) and >10 pack-years of smoking exposure (n = 44)	Mean age 67.2 \pm 8.1 y; 54% male and 37% received LTOT	Spirometry/home PSG	AHI ≥ 5	>3%	65.9%
Staveling et al., 2014 [50]	Switzerland	Consecutive patients with confirmed COPD from outpatient clinic (n = 177)	Mean age 64 y & range 42–90 y; 63% male	Spirometry/home PSG	AHI > 10	>4%	19.0%
Turcani et al., 2014 [31]	Czech Republic	Consecutive patients hospitalized for COPD exacerbations (n = 35)	Median age of 66 y	Physician/lab PSG	AHI ≥ 5	$\geq 3\%$	51%
Venkateswaran et al., 2014 [51]	Singapore	COPD patients aged ≥ 40 y were recruited from hospital (n = 22)	Mean age 71 \pm 9 y; 86% male	Physician/lab PSG	AHI ≥ 5		63.6%

Σύνδρομο αλληλοεπικάλυψης ΧΑΠ-ΣΑΥ (overlap syndrome)



Για παράδειγμα, οι ασθενείς με ΧΑΠ έχουν συχνά μυοπάθεια των σκελετικών μυών, είτε ως αποτέλεσμα της νόσου και του καπνίσματος είτε ως αποτέλεσμα της μακράς θεραπείας με κορτικοειδή, με αποτέλεσμα τη δυσλειτουργία των διατεινόντων μυών του ανώτερου αεραγωγού και την προδιάθεση για ΣΑΥ

Από την άλλη πλευρά, σε ένα πειραματικό μοντέλο φάνηκε ότι η επαναλαμβανόμενη σύγκλειση του ανώτερου αεραγωγού, όπως συμβαίνει σε ασθενείς με ΣΑΥ, αυξάνει την αντίσταση του κατώτερου αεραγωγού και οδηγεί σε απόφραξη

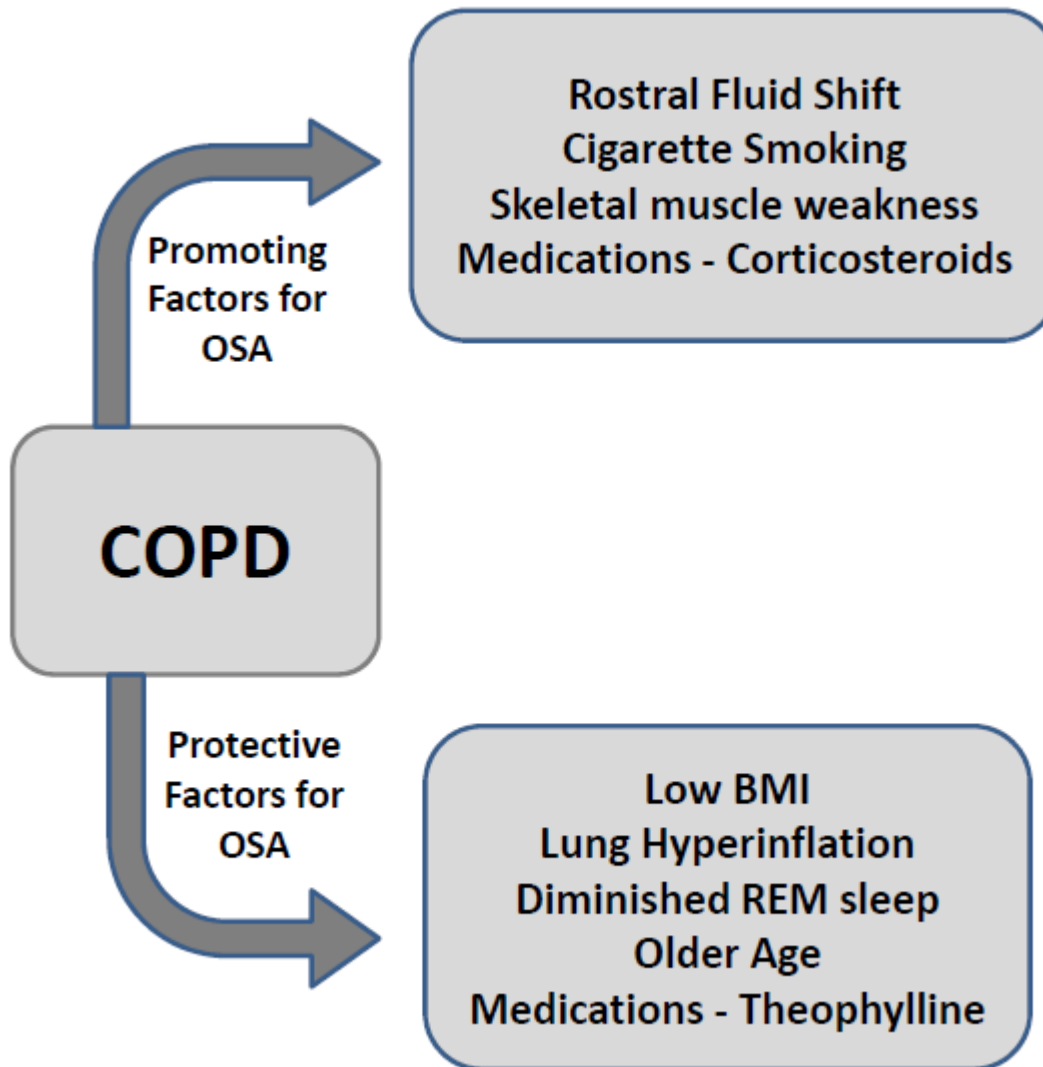
Agustí AGN et al. Skeletal muscle apoptosis and weight loss in chronic obstructive pulmonary disease.

Am J Respir Crit Care Med 2002;166:485–489

Nadel JA, Widdicombe JG: Reflex effects of upper airway irritation on total lung resistance and blood pressure.

J Appl Physiol 1962;17:861–865

Σύνδρομο αλληλοεπικάλυψης ΧΑΠ-ΣΑΥ (overlap syndrome)

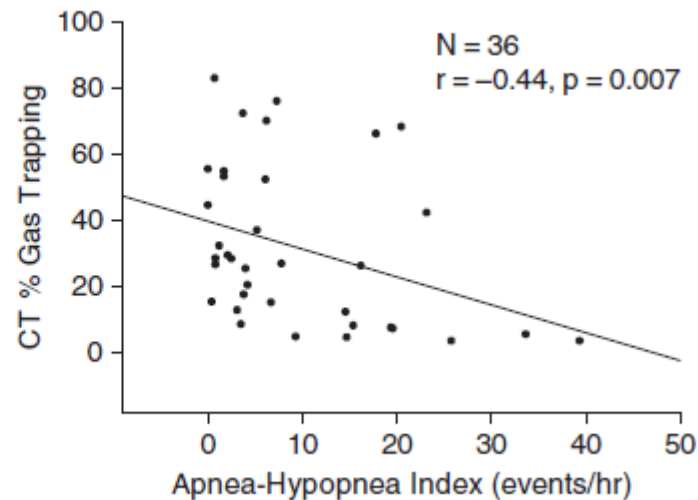
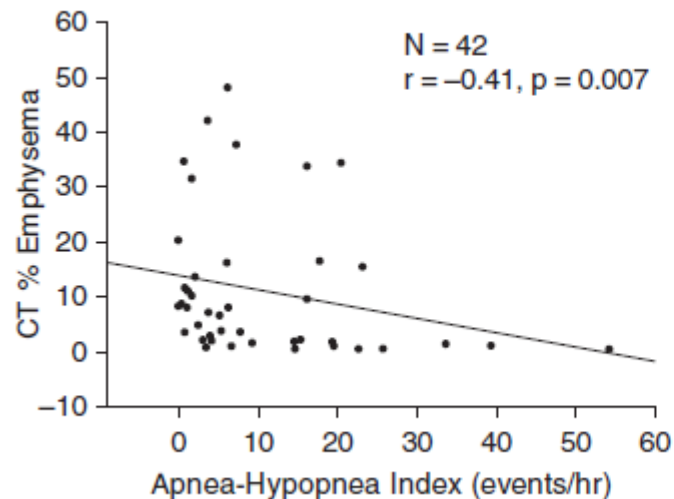


Effect of Emphysema Severity on the Apnea–Hypopnea Index in Smokers with Obstructive Sleep Apnea

Samuel L. Krachman¹, Rachna Tiwari¹, Maria Elena Vega¹, Daohai Yu¹, Xavier Soler², Fredric Jaffe¹, Victor Kim¹, Irene Swift¹, Gilbert E. D'Alonzo¹, Gerard J. Criner¹, and the COPDGene Investigators

¹Department of Pulmonary, Critical Care, and Sleep Medicine, Temple University School of Medicine, Philadelphia, Pennsylvania; ²Department of Pulmonary, Critical Care, and Sleep Medicine University of California, San Diego, San Diego, California

AnnalsATS Volume 13 Number 7 | July 2016





Sleep Apnea Clinical Score, Berlin Questionnaire, or Epworth Sleepiness Scale: which is the best obstructive sleep apnea predictor in patients with COPD?

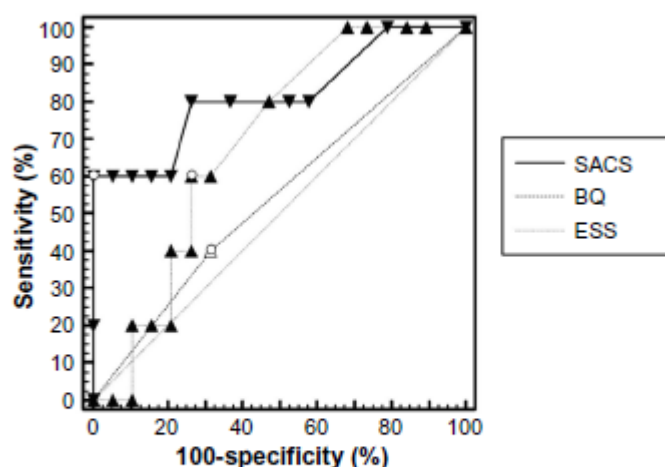


Figure 2 ROC curves for SACS, BQ, and ESS.

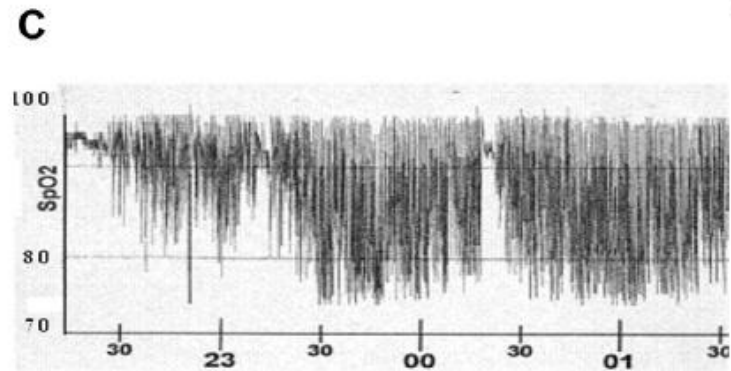
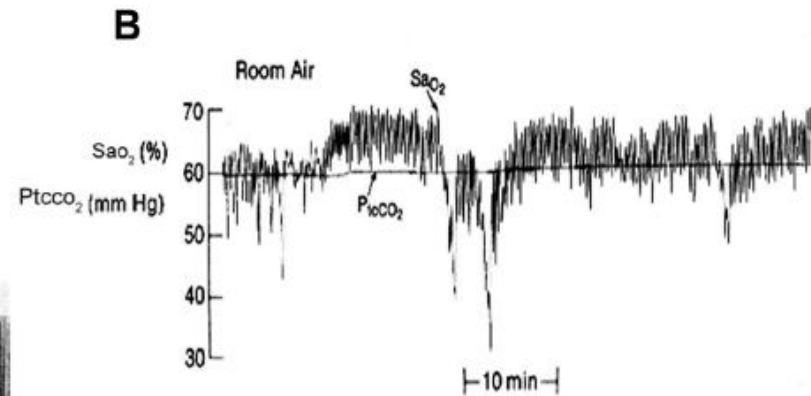
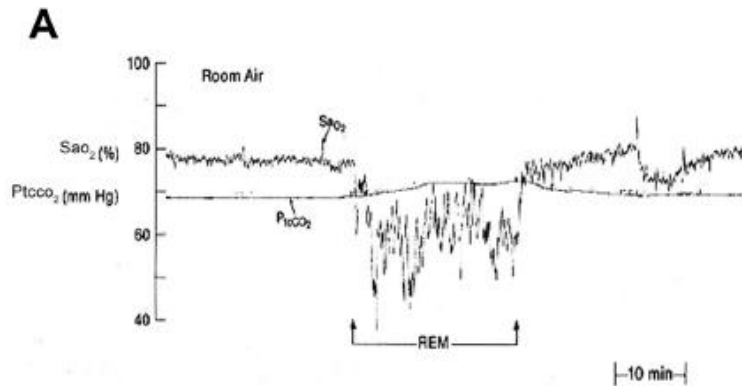
Abbreviations: BQ, Berlin Questionnaire; ESS, Epworth Sleepiness Scale; ROC, receiver-operating characteristic; SACS, Sleep Apnea Clinical Score.

Διάγνωση ΣΑΥ σε ασθενείς με ΧΑΠ



- Νυχτερινή οξυμετρία: ο υπολογισμός του δείκτη αποκορεσμού βοηθάει στο screening ασθενών με υψηλή pre-test probability για ΣΑΥ
- Η χρήση της οξυμετρίας ως εργαλείο προσυμπτωματικού ελέγχου έχει μικρότερη αξία στο μέτριο- βαρύ ΣΑΥ
- Νυχτερινή μέτρηση end tidal/ transcutaneous CO₂
- Gold standard: PSG

Διάγνωση ΣΑΥ σε ασθενείς με ΧΑΠ





Current evidence on prevalence and clinical outcomes of co-morbid obstructive sleep apnea and chronic obstructive pulmonary disease: A systematic review

Md Shajedur R. Shawon ^a, Jennifer L. Perret ^{c,d}, Chamara V. Senaratna ^{c,e}, Caroline Lodge ^c, Garun S. Hamilton ^{b,1,*}, Shyamali C. Dharmage ^{c,1}

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Polysomnographic findings of overlap syndrome patients in comparison to OSA alone patients.

Authors, year, references	Sleep parameters	Overlap syndrome	OSA only	Remarks
Azuma et al., 2014 [20]	AHI (per hour)	14.2 ± 8.6	16.1 ± 11.9	
	SaO ₂ (Mean)	95.9 ± 1.3	95.4 ± 1.7	
	SaO ₂ nadir	80.6 ± 11.2	81.2 ± 7.3	
Bednarek et al., 2005 [18]	AHI (per hour)	19.0	25.3	NS
	SaO ₂ (Mean)	89.6	92.3	P = 0.00
	T90 (%)	25.4	18.2	P = 0.04
Chaouat et al., 1995 [7]	AHI (per hour)	89 ± 37	76 ± 32	NS
	SaO ₂ (Mean)	89 ± 4	91 ± 4	P < 0.05
	SaO ₂ nadir	84 ± 7	86 ± 6	NS
	Time spent in apnea/total sleep time ratio (%)	22 ± 15	24 ± 18	NS
Greenberg-Dotan et al., 2014 [34]	AHI (per hour)	41 ± 25	34 ± 25	P = 0.09
	T90 (%)	28 ± 32	14 ± 25	P = 0.02
	Sleep efficiency (%)	77 ± 14	79 ± 19	P = 0.69
Hawrylkiewicz et al., 2004 [32]	AHI (per hour)	64 ± 19	62 ± 22	
	SaO ₂ (Mean)	80.2 ± 8.5	87.4 ± 5.4	
	SaO ₂ nadir	50.7 ± 19.7	57.4 ± 15.9	
	T90 (%)	76.9 ± 25.7	48.3 ± 25.4	
Rizzi et al., 1997 [33]	AHI (per hour)	31 ± 16	40 ± 11	P = 0.05
	SaO ₂ (Mean)	89 ± 5	92 ± 5	P = 0.05
	SaO ₂ nadir	75 ± 12	72 ± 16	NS
	Sleep efficiency (% sleep time)	78 ± 14	85 ± 14	P = 0.05
Sanders et al., 2003 [19]	Odds ratio of having > 5% total sleep time spent with SpO ₂ < 90% in compared to normal individuals after adjusting for possible confounders	8.06 (95% CI 5.55–11.69)	8.98 (95% CI 6.86–11.74)	
Shiina et al., 2012 [26]	AHI (per hour)	30.9	33.7	P = 0.18
	SaO ₂ (mean)	95.0	95.0	P = 0.63
	SaO ₂ nadir	81.0	81.0	P = 0.18
	Sleep efficiency (% sleep time)	78.5	83.9	P < 0.01

How is the Overlap Syndrome Different than COPD or OSA?



- Patients with the Overlap Syndrome have increased risk of complications compared to those with COPD or OSA alone

*Gan WQ Thorax, 2004
Greenberg-Dotan S, Sleep Breath 2013*

- Respiratory failure
- Pulmonary hypertension
- Hypoventilation
- More severe hypoxemia
- Diabetes
- Obesity
- Death



Coexistence of OSA may compensate for sleep related reduction in neural respiratory drive in patients with COPD

Bai-Ting He,¹ Gan Lu,² Si-Chang Xiao,¹ Rui Chen,³ Joerg Steier,⁴ John Moxham,⁴
Michael I Polkey,⁵ Yuan-Ming Luo¹

He B-T, et al. *Thorax* 2017;**72**:256–262. doi:10.1136/thoraxjnl-2016-208467

Key messages

What is the key question?

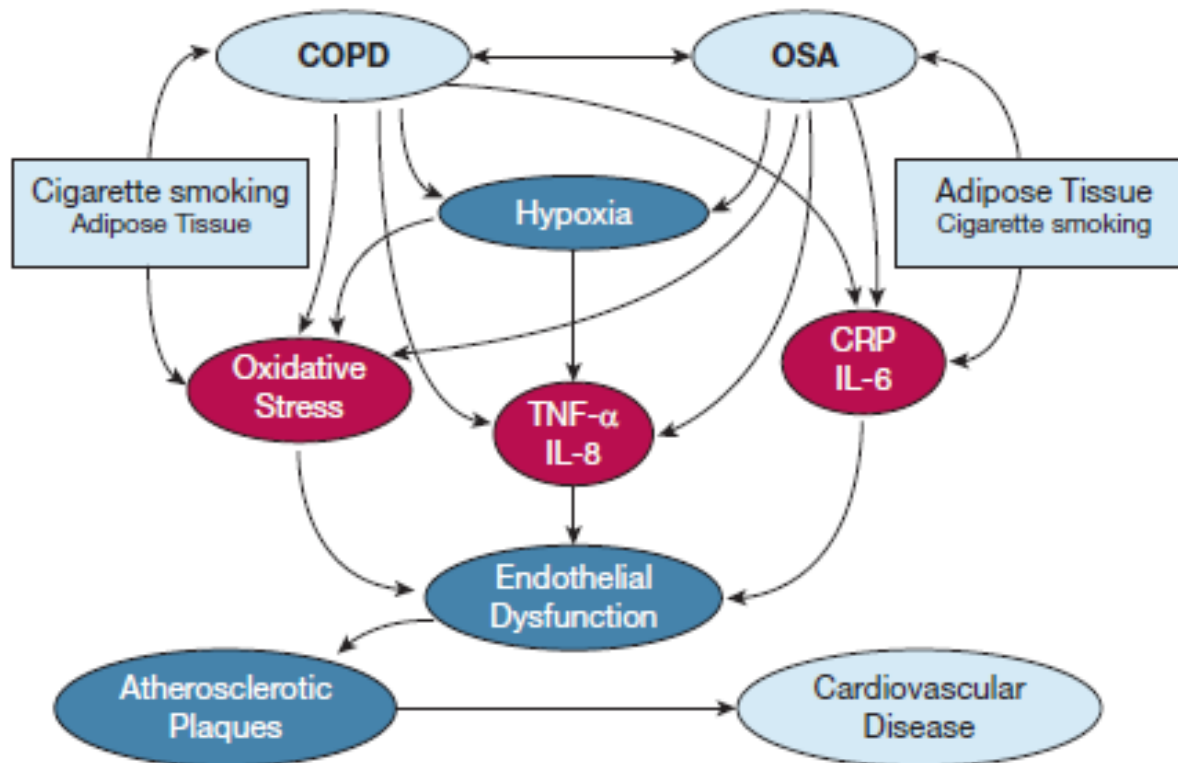
- ▶ The mechanisms underlying sleep-related hypoventilation in patients with coexistent COPD and obstructive sleep apnoea (OSA), an overlap syndrome, are unknown.

What is the bottom line?

- ▶ This study shows that sleep-related hypoventilation in patients with overlap syndrome is due to an increase in upper airway resistance associated with OSA rather than reduction of neural respiratory drive associated with COPD.

Why read on?

- ▶ Sleep-related hypoventilation in patients with COPD alone mainly occurs because of a decrease in neural respiratory drive whereas it is mainly a result of an increase in upper airway resistance in patients with overlap syndrome.



Current evidence on prevalence and clinical outcomes of co-morbid obstructive sleep apnea and chronic obstructive pulmonary disease: A systematic review



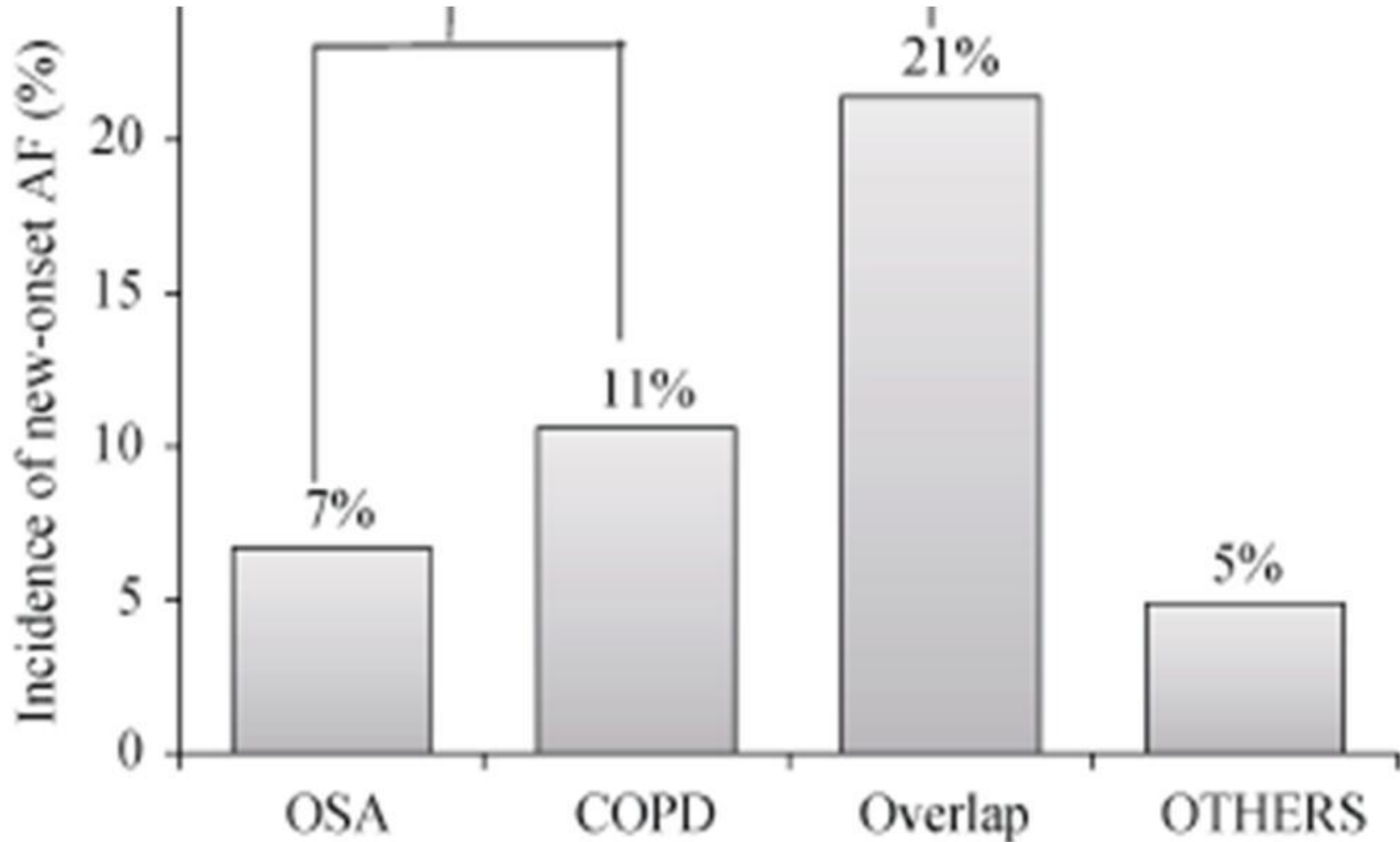
Md Shajedur R. Shawon ^a, Jennifer L. Perret ^{c,d}, Chamara V. Senaratna ^{c,e}, Caroline Lodge ^c, Garun S. Hamilton ^{b,1,*}, Shyamali C. Dharmage ^{c,1}

Sleep Medicine Reviews 32 (2017) 58–68

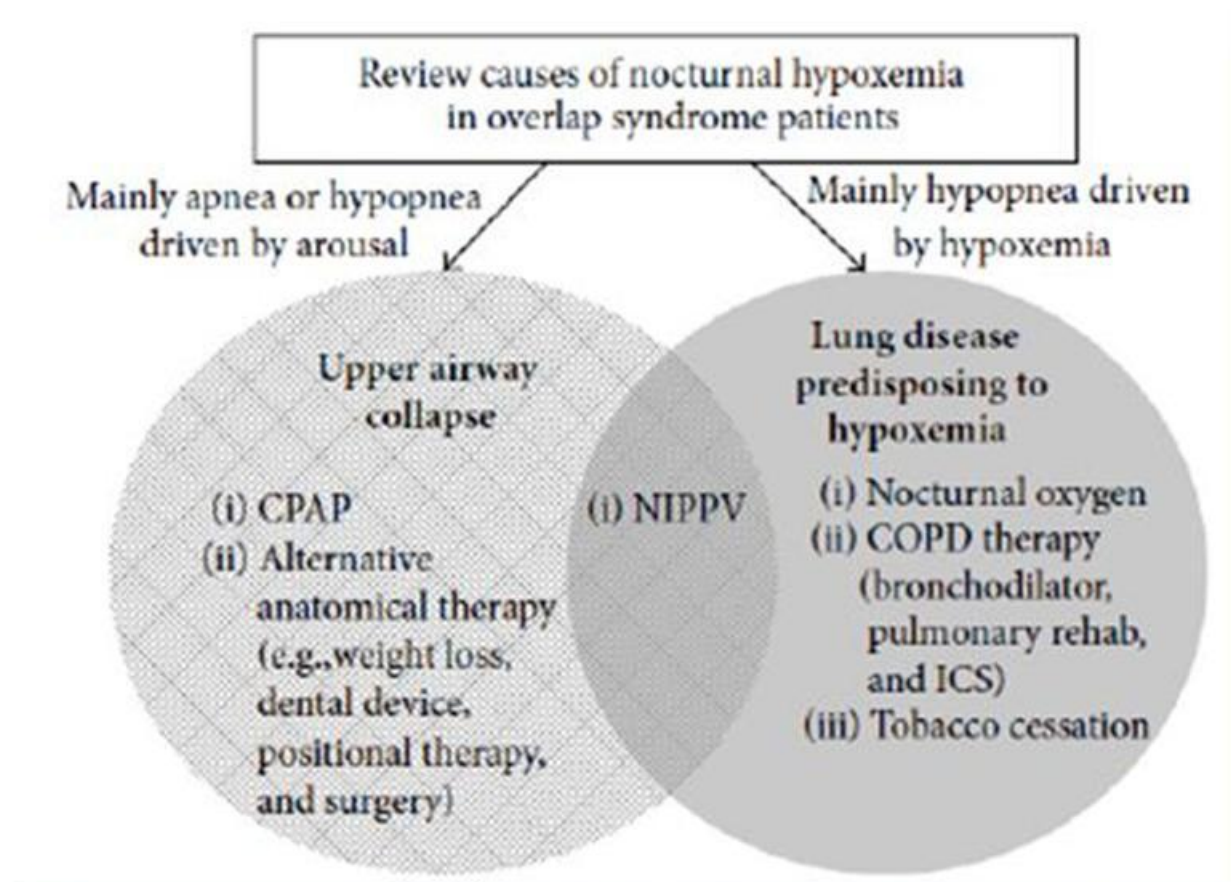
Clinical outcomes of overlap syndrome.

Outcomes	Authors, year, references	Country	Study design	Study population	Confounders adjusted for	Main findings
Cardiovascular disease	Chaouat et al., 1995 [7]	France	Cross-sectional	Consecutively recruited sleep lab patients (n = 265)	PaO ₂ , PaCO ₂ , FEV1	OS patients had significantly higher pulmonary hypertension than OSA patients (42% vs. 13%; p < 0.001)
	Ganga et al., 2013 [21]	USA	Retrospective cohort with 2 y follow-up	Consecutive recruited elderly (≥65 y) from inpatients (n = 2873)	Age, male, COPD, heart failure, valvular disorders, hypertension, chronic kidney disease	Incidence of new-onset atrial fibrillation was significantly higher in OS patients than OSA patients (21.4% vs. 6.7%; P < 0.05). Odds ratio: 3.66, 95% CI: 1.056–6.860, (P = 0.007)
	Hawrylkiewicz et al., 2004 [32]	Poland	Cross-sectional	67 OSA patients and 17 overlap syndrome patients		The occurrence of pulmonary hypertension was higher in OS patients than OSA patients (82% vs. 16%). Pulmonary hypertension did not correlate with severity of nocturnal desaturation
	Sharma et al., 2013 [35]	USA	Cross-sectional	18 COPD patients included and seven of them had overlap syndrome		RVMI was significantly higher in overlap patients than COPD only patients (19 ± 6 versus 11 ± 6; p = 0.02)
On quality of life	Mermigkiset al., 2007 [12]	Greece	Case-control	30 OS patients and 15 age-matched COPD controls		Overlap syndrome patients had significantly lower quality of life (as measured by St. George's respiratory questionnaire) than the controls
	Zohal et al., 2014 [49]	Iran	Cross-sectional	139 COPD patients were included and assessed for OS		OS patients had worse quality of life (score 60.6 ± 10.4) than COPD patients (score 50.6 ± 10.4)

Overlap patients at greater risk for AF than OSA or COPD alone



Θεραπευτικές επιλογές



Current evidence on prevalence and clinical outcomes of co-morbid obstructive sleep apnea and chronic obstructive pulmonary disease: A systematic review



Md Shajedur R. Shawon^a, Jennifer L. Perret^{c, d}, Chamara V. Senaratna^{c, e}, Caroline Lodge^c, Garun S. Hamilton^{b, 1, *}, Shyamali C. Dharmage^{c, 1}

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On mortality	Machado et al., 2010 [29]	Brazil	Prospective cohort with 10 y follow-up	95 COPD patients receiving LTOT and concurrently diagnosed with OSA. 61 received CPAP and 34 did not	Age, smoking history, obesity, CPAP, PaO ₂ , PaCO ₂ , bronchodilator, FEV1, AHI, T90	5 y survival was significantly higher in CPAP-treated patients (71%) compared to the non-treated group (26%) (p < 0.0001). The hazard ratio for death in CPAP-treated versus non-treated patients was 0.19 (95% CI 0.08–0.48).
	Marin et al., 2010 [13]	Spain	Prospective cohort with median follow-up of 9.4 y	228 patients with OS treated with CPAP, 213 patients with OS not treated with CPAP, and 210 COPD-only patients	Age, BMI, current smoker, alcohol use, Charlson index, severity of COPD, COPD exacerbation, COPD group, ESS	Patients with overlap syndrome not treated with CPAP had a higher mortality (relative risk, 1.79; 95% CI: 1.16–2.77) versus the COPD-only group. Hours of CPAP use and age were independent predictors of mortality (HR 0.71 and 1.14, p < 0.001, 0.002).
	Stanchina et al., 2013 [22]	USA	Prospective cohort	227 patients with overlap syndrome treated with CPAP.	CPAP, gender, FEV1, AHI, BMI, age, tobacco active use, Charlson index	Patients with overlap syndrome not treated with CPAP were more likely to suffer a severe COPD exacerbation leading to
COPD exacerbation	Marin et al., 2010 [13]	Spain	Prospective cohort with median follow-up of 9.4 y	228 patients with OS treated with CPAP, 213 patients with OS not treated with CPAP, and 210 COPD-only patients	Age, BMI, current smoker, alcohol use, Charlson index, severity of COPD, COPD exacerbation, COPD group, ESS	Patients with overlap syndrome not treated with CPAP were more likely to suffer a severe COPD exacerbation leading to



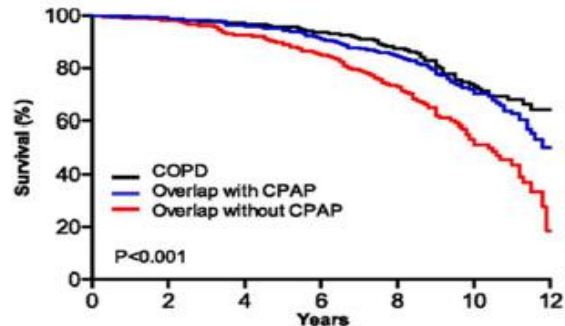
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Md Shajedur R. Shawon ^a, Jennifer L. Perret ^{c, d}, Chamara V. Senaratna ^{c, e}, Caroline Lodge ^c, Garun S. Hamilton ^{b, 1, *}, Shyamali C. Dharmage ^{c, 1}

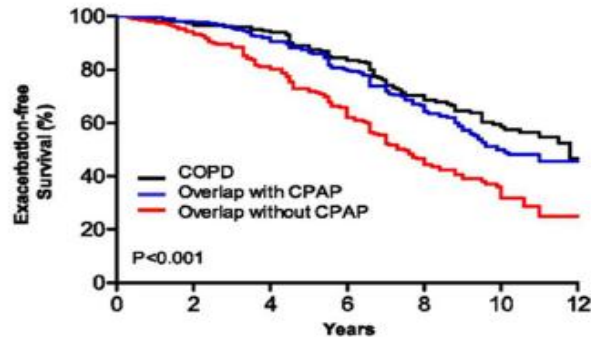
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Outcomes	Authors, year, references	Country	Study design	Study population	Confounders adjusted for	Main findings
Medical utilization and costs	Shaya et al., 2009 [15]	USA	Prospective cohort	3455 COPD patients from which 2.87% had concomitant diagnosis of OSA	Age, gender, race, obesity, Charlson index, and number of days in cohort	hospitalization (relative risk, 1.70; 95% CI: 1.21–2.38) versus the COPD-only group. OS patients had greater medical utilizations (13.4 vs. 8.2) compared to COPD ($p < 0.001$). Mean overall annual costs for OS patients were significantly higher (\$8903 vs. \$4748) than COPD only group. ($p = 0.035$)

Σύνδρομο αλληλοεπικάλυψης ΧΑΠ-ΣΑΥ (overlap syndrome)



No at risk	210	203	196	184	144	89	10
COPD	228	223	215	201	167	97	8
Overlap with CPAP	213	204	186	161	121	57	3
Overlap without CPAP							



No at risk	210	199	189	158	107	47	6
COPD	228	222	202	168	114	41	5
Overlap with CPAP	213	197	165	124	66	24	2
Overlap without CPAP							

Αποτελεσματικότητα θεραπείας με CPAP

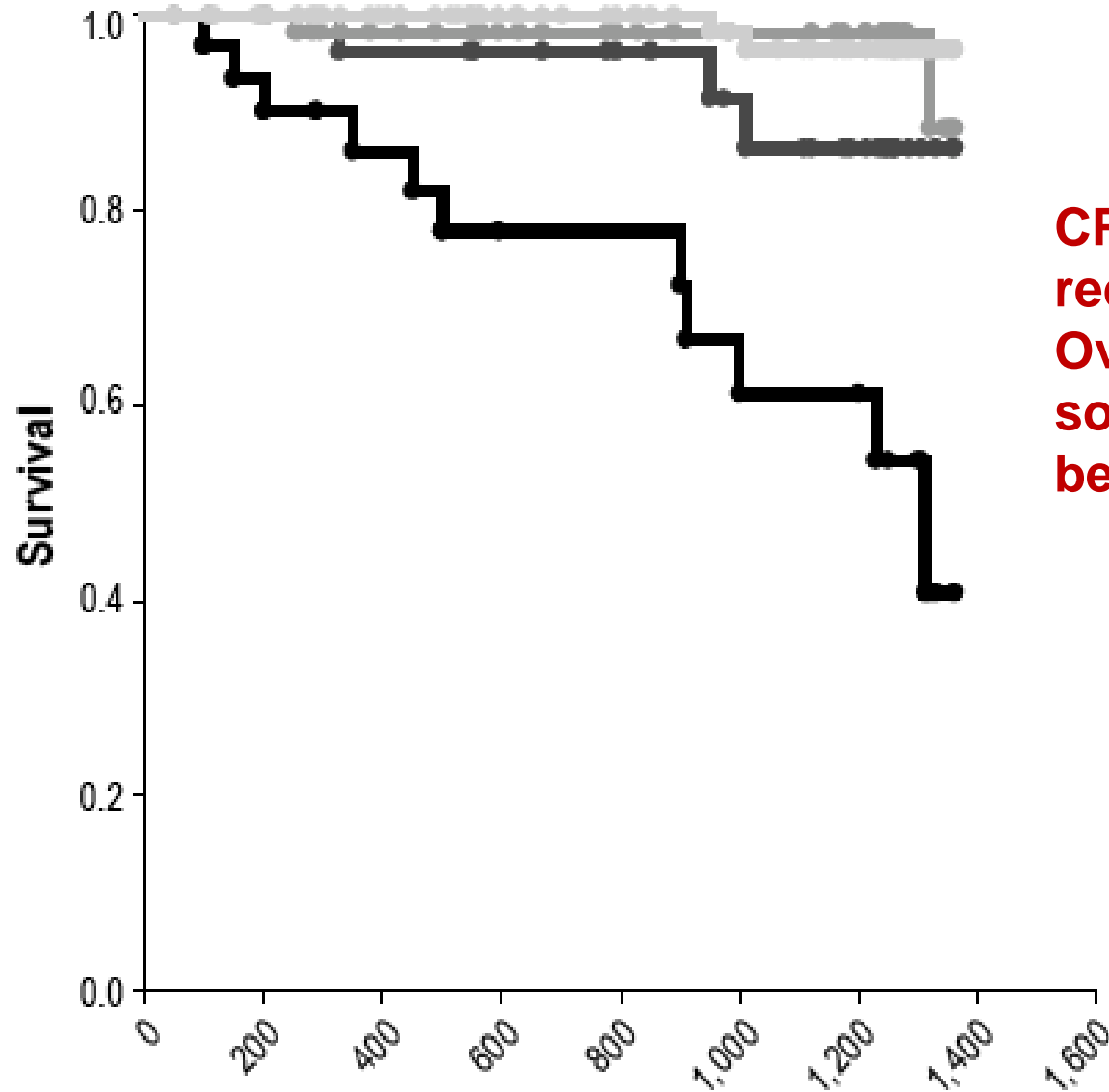
Marin JM, Soriano JB, Carrizo SJ, et al. Outcomes in Patients with Chronic Obstructive Pulmonary

Disease and Obstructive Sleep Apnea. American Journal of Respiratory and Critical Care

Medicine 2010; 182:325-331



Hours of CPAP use: 0-2 2-4 4-6 6-8

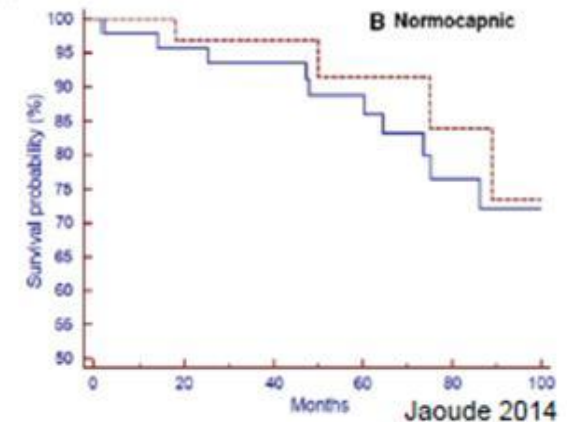
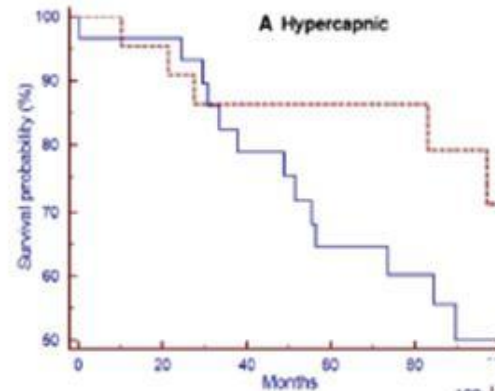


CPAP use is associated with reduced mortality in the Overlap Syndrome, and some use (2-4 hours) is better than none.

CLINICAL FEATURES AND TREATMENT EFFECTS



- **Quality of life**
 - High burden of nocturnal symptoms
 - Not influenced by other therapies
 - PR
 - Bronchodilators
- **Exacerbations**
 - Reduced frequency in compliant patients
- **Mortality**
 - Dose response effect
 - Effect most pronounced in hypercapnic patients



CLINICAL FEATURES AND TREATMENT EFFECTS



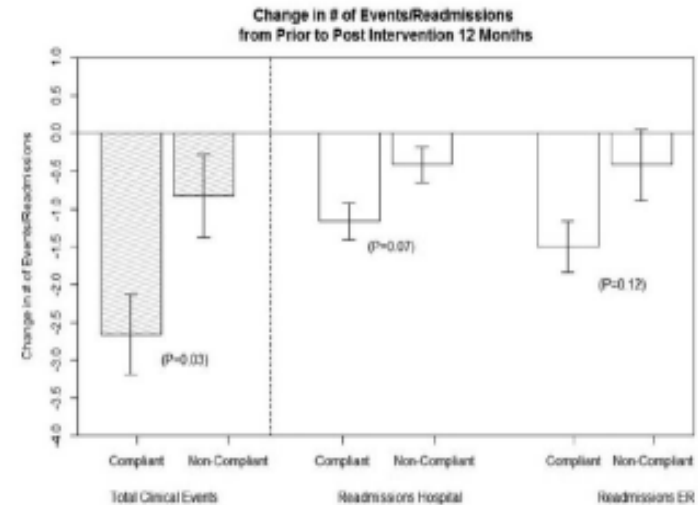
- **Quality of life**

- High burden of nocturnal symptoms
- Not influenced by other therapies
 - PR
 - Bronchodilators

- **Exacerbations**

- Reduced frequency in compliant patients

- **Mortality**



THE GUIDELINES SAY...



Practice Parameters for the Use of Autotitrating Continuous Positive Airway Pressure Devices for Titrating Pressures and Treating Adult Patients with Obstructive Sleep Apnea Syndrome: An Update for 2007

An American Academy of Sleep Medicine Report

3. RECOMMENDATIONS

3.2. Patients with congestive heart failure, significant lung disease such as chronic obstructive pulmonary disease, patients expected to have nocturnal arterial oxyhemoglobin desaturation due to conditions other than OSA (e.g., obesity hypoventilation syndrome), patients who do not snore (either naturally or as a result of palate surgery), and patients who have central sleep apnea syndromes are not currently candidates for APAP titration or treatment. (Standard)

This recommendation is unchanged from the previous parameter paper.⁶ Most studies evaluating APAP, regardless of the technology used, exclude such patients because the sensors and algorithms identifying respiratory events may not be sensitive or specific under these circumstances.

4.0 AREAS FOR FUTURE RESEARCH

4.1 In order for APAP to better apply to usual clinical circumstances, studies are needed that clarify which patients can and cannot be served by APAP devices, with particular attention to subjects with mild OSA or comorbidities.

NIV for COPD



- Can improve gas exchange during wakefulness
- Can improve sleep quality

Meecham Jones DJ Am J Respir Crit Care Med 1995

- Can be withdrawn for up to 2 weeks without deterioration in daytime ABGs

Masa Jimenez JF Chest 1995

- Can reduce need for intubation and mechanical ventilation in COPD exacerbations

Brochard L NEJM 1995

- May improve dyspnea and QoL

Bhatt SP Intrn J COPD

- Is associated with improved mortality in retrospective trials, but not RCTs.
- Controversy exists about whether to use high-intensity (rate) or high pressure settings.

Έλεγχος ασθενών ΧΑΠ για ΣΑΥ

Πότε πρέπει να γίνεται;



- Υπερκαπνία στην εγρήγορση δυσανάλογα υψηλή σε σχέση με την απόφραξη
- Μέτριος- σοβαρός νυχτερινός αποκορεσμός
- Πνευμονική υπέρταση και AF
- Χαμηλότερος αναπνεόμενος όγκος και υψηλότερος αναπνευστικός ρυθμός στο overlap

Radwan L et al. Eur Respir J 1995

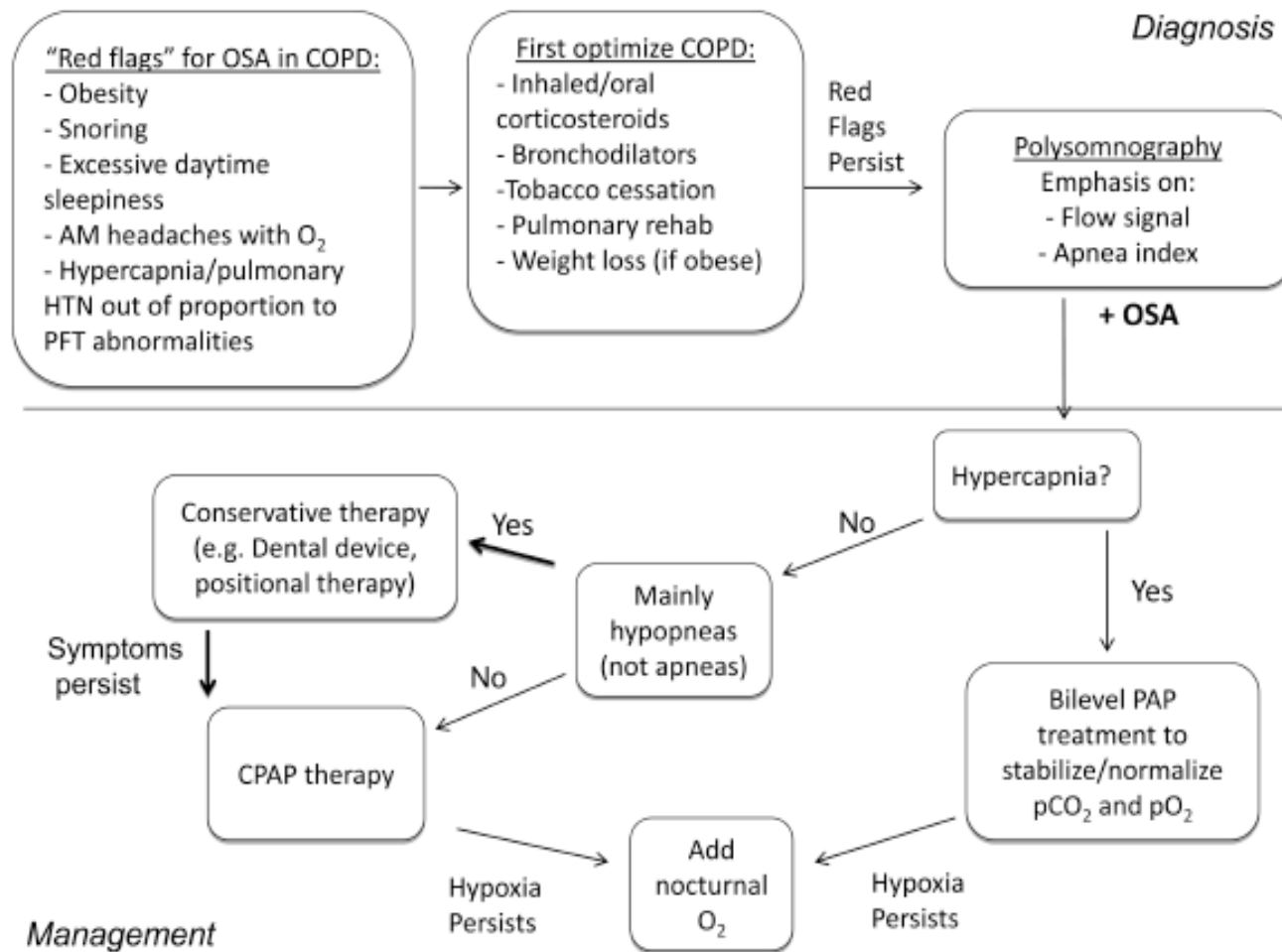


Figure 3. Management algorithm for patients with COPD

Patients with COPD should be assessed for any "red flags" that might suggest the presence of concurrent OSA. If present, COPD should be optimized prior to undergoing polysomnography. Attention should be paid to the flow signal and apnea index when assessing the severity of OSA. If hypercapnia is present, the patient can begin on BiLevel positive airway pressure. If flow limitation is present without significant apneas, conservative therapy such as a mandibular advancement device, weight loss, and positional therapy should be considered. If apneas predominate, CPAP should be started. Supplemental oxygen should be added if hypoxemia persists.

Summary/Conclusions



- Sleep and COPD have adverse effects on each other (exacerbation, CV comorbidity, mortality)
- COPD + OSA (Overlap Syndrome) is best treated with CPAP
- NIV shows promise, but is still poorly studied and expensive