ΧΑΠ και ΄Υπνος

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Medical School, University of Crete

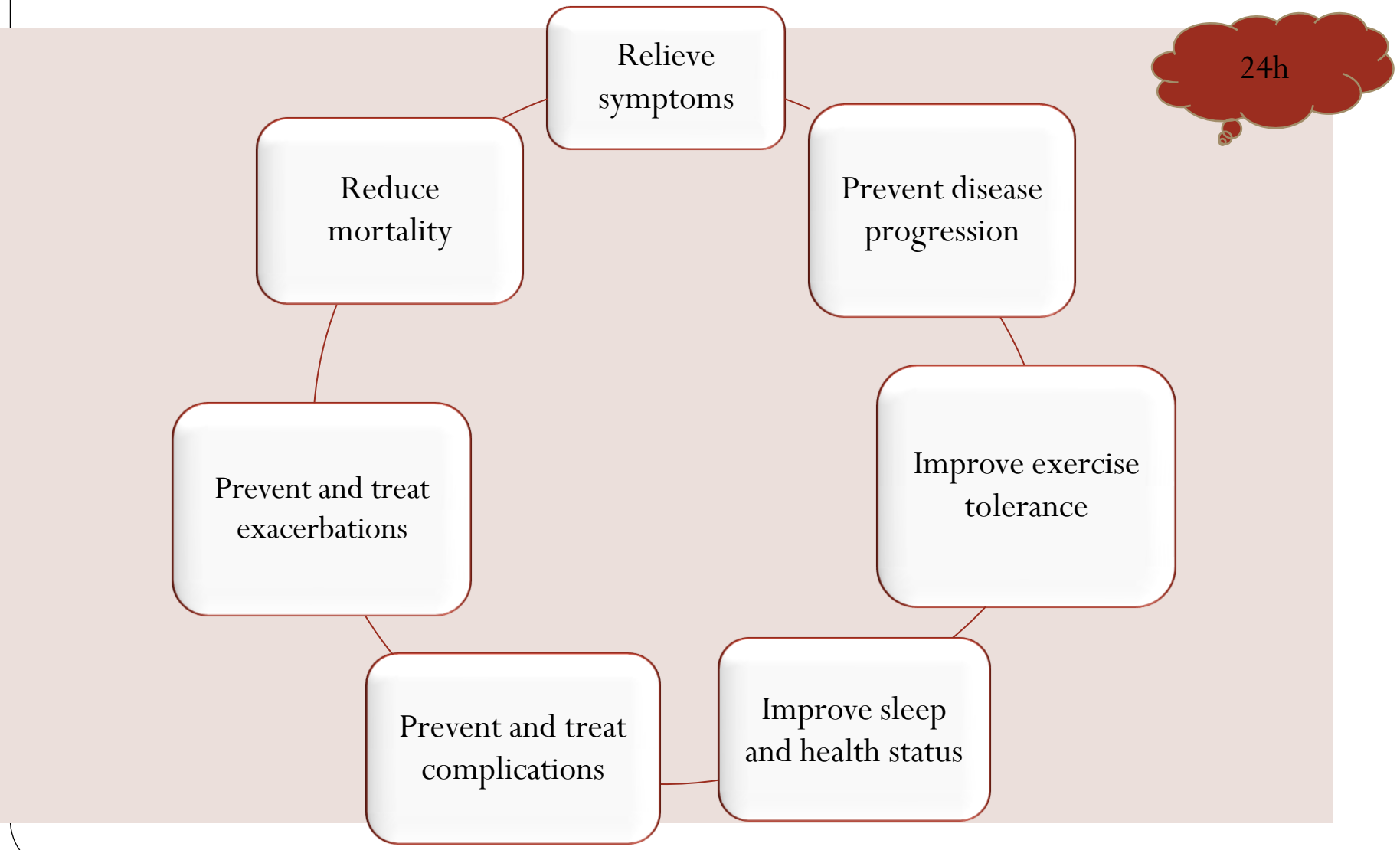
Στο Γιατρό, το συνάδελφο, το Δάσκαλο,
το φίλο.

Ευχαριστούμε!!!!!!!!!!!!

Definition of COPD

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and **influenced by host factors including abnormal lung development. Significant comorbidities may have an impact on morbidity and mortality.**

Goals of effective management



MANAGEMENT OF COPD

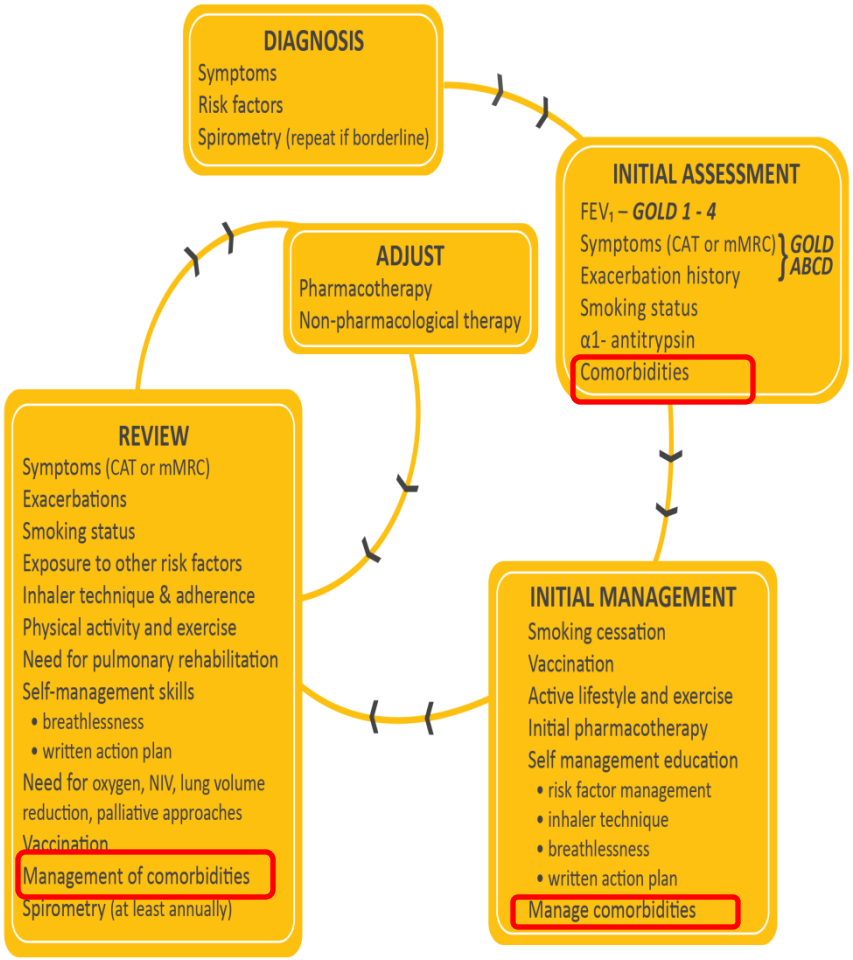


FIGURE 4.1

FOLLOW-UP OF NON-PHARMACOLOGICAL TREATMENT

1. IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT AND OFFER:

- Flu vaccination every year and other recommended vaccinations according to guidelines
- Self-management education
- Assessment of behavioral risk factors such as smoking cessation (if applicable) and environmental exposures

Ensure

- Maintenance of exercise program and physical activity
- Adequate sleep and a healthy diet

2. IF NOT, CONSIDER THE PREDOMINANT TREATABLE TRAIT TO TARGET

• DYSPNEA •

- Self-management education (written action plan) with integrated self-management regarding:
  - Breathlessness and energy conservation techniques, and stress management strategies
- Pulmonary rehabilitation (PR) program and/or maintenance exercise program post PR

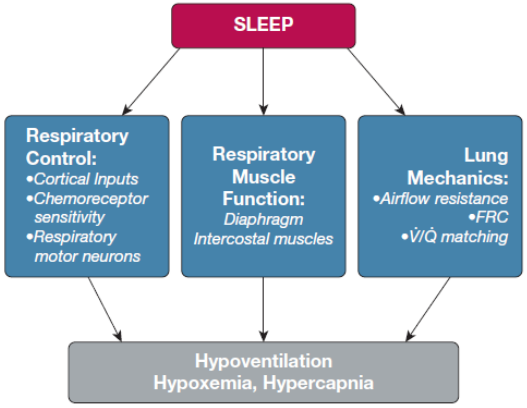
• EXACERBATIONS •

- Self-management education (written action plan) that is personalized with respect to:
  - Avoidance of aggravating factors
  - How to monitor/manage worsening of symptoms
  - Contact information in the event of an exacerbation

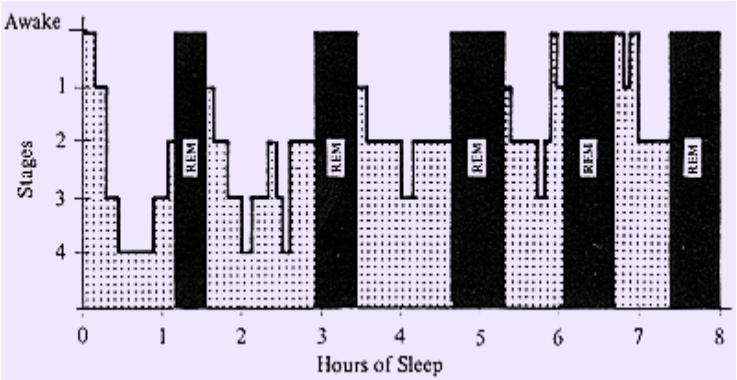
All patients with advanced COPD should be considered for end of life and palliative care support to optimize symptom control and allow patients and their families to make informed choices about future management

TABLE 4.9

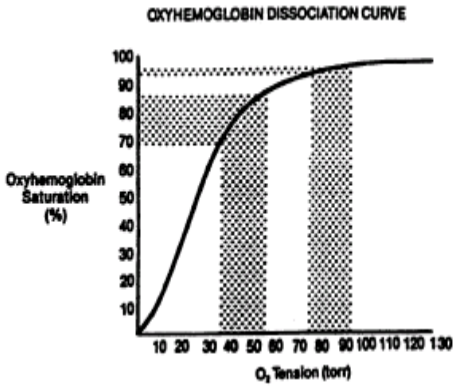
Επίδραση του ύπνου στην αναπνοή

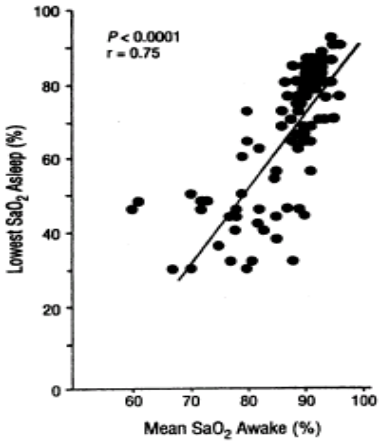


- **Σε ποιό στάδιο του ύπνου βρισκόμαστε;;**



Σε ποιά θέση της καμπύλης βρισκόμαστε κατά την έναρξη του ύπνου;;





Pubmed: Sleep Disorders AND COPD, την τελευταία 5ετία: >550 papers

REVIEW
SLEEP AND BREATHING

Sleep disorders in COPD: the forgotten dimension

Walter T. McNicholas[1], Johan Verbraecken[2] and Jose M. Marin[3]

Eur Respir Rev 2013; 22: 365–375 |

EXPERT REVIEWS

Sleep-related disorders in chronic obstructive pulmonary disease

Expert Rev. Respir. Med. 8(1), 79–88 (2014)

Review Article

Chronic obstructive pulmonary disease and obstructive sleep apnoea—the overlap syndrome

Walter T. McNicholas

Department of Respiratory and Sleep Medicine, St. Vincent's University Hospital, Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Dublin, Ireland

Correspondence to: Prof. Walter T. McNicholas, MD. Pulmonary and Sleep Disorders Unit, St. Vincent's University Hospital, Elm Park, Dublin 4, Ireland. Email: walter.mcnicholas@ucd.ie.

Abstract: Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA) are highly prevalent disorders and the co-existence of both disorders, termed the overlap syndrome, affects at least 1% of the adult population. Patients with the overlap syndrome typically experience more pronounced nocturnal oxygen desaturation and there is a high prevalence of pulmonary hypertension in such patients. Recent evidence suggests that the prevalence of each disorder together is higher than might be predicted by simple prevalence statistics, although the evidence is not clear-cut in this regard. Sleep itself can have several negative effects in patients with COPD. Sleep quality is diminished with reduced amounts of slow wave and rapid-eye-movement (REM) sleep, which may contribute to daytime symptoms such as fatigue and lethargy. Furthermore, normal physiological adaptations during sleep that result in mild hypoventilation in normal subjects are more pronounced in COPD, which can result in clinically important nocturnal oxygen desaturation. Management of sleep disorders in patients with COPD should address both sleep quality and disordered gas exchange. Non-invasive pressure support is beneficial in selected cases, particularly during acute exacerbations associated with respiratory failure, and is particularly helpful in patients with the overlap syndrome. There is limited evidence of benefit from pressure support in the chronic setting in COPD patients without OSA.

J Thorac Dis 2016;8(2):236–242

Hindawi Publishing Corporation
Canadian Respiratory Journal
Volume 2016, Article ID 7947198, 5 pages
http://dx.doi.org/10.1155/2016/7947198

Hindawi

Review Article

Sleep in Chronic Obstructive Pulmonary Disease: Evidence Gaps and Challenges

Rachel Jen,[1,2] Yanru Li,[3] Robert L. Owens,[2] and Atul Malhotra[2]

ORIGINAL ARTICLE
COPD

Prevalence of night-time dyspnoea in COPD and its implications for prognosis

Peter Lange[1,2,3,4], Jacob Louis Marott[3], Jørgen Vestbo[5,6] and Børge Grønne Nordestgaard[3,4,7,8]

Eur Respir J 2014; 43: 1590–1598 | DOI: 10.1183/09031936.00196713

AMERICAN THORACIC SOCIETY DOCUMENTS

Research Priorities in Pathophysiology for Sleep-disordered Breathing in Patients with Chronic Obstructive Pulmonary Disease

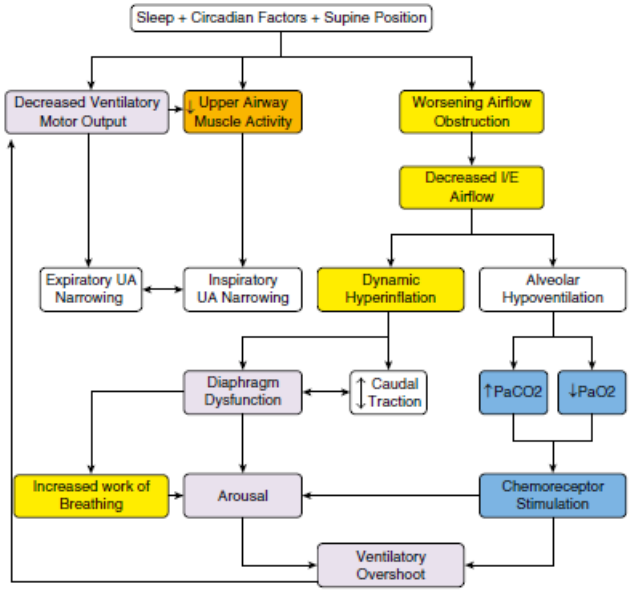
An Official American Thoracic Society Research Statement

Atul Malhotra, Alan R. Schwartz, Hartmut Schneider, Robert L. Owens, Pamela DeYoung, MeiLan K. Han, Jadwiga A. Wedzicha, Nadia N. Hansel, Michelle R. Zeidler, Kevin C. Wilson, and M. Safwan Badr; on behalf of the ATS Assembly on Sleep and Respiratory Neurobiology

This official Research Statement of the American Thoracic Society was approved December 2017

Am J Respir Crit Care Med Vol 197, Iss 3, pp 289–299, Feb 1, 2018

Sleep: a period for **vulnerability** for COPD patients!!!!



Am J Respir Crit Care Med Vol 197, Iss 3, pp 289–299, Feb 1, 2018

- **First**: loss of "wakefulness drive to breath", reduced hypercapnic and hypoxic chemo sensitivity and muscle atonia during REM with the flattening of diaphragm resulted in desaturations and hypoventilation

  27-70% COPD pts with awake SaO2: 90-95% experience nocturnal hypoxemia → Sleep hypoventilation

- **Second**: cough is suppressed during sleep leading to mucus plugging and hypersecretion, affecting nocturnal gas exchange and leading to productive cough in the morning

- **Third**: Overlap syndrome (OSA and COPD) associated with poor prognosis

- >60% of COPD pts experience sleep symptoms and/or bothersome dyspnea/cough at night, often underreported and not part of routine clinical management

Sleep quality in COPD - EEG

- PSGs

  Alterations in macro and micro architecture (changes of sleep-stage transitions and microarousals)

  - ↓ SWS και REM sleep
  - ↓ Sleep efficiency (50–70%), ↓ TST
  - 2014 May 15;10(5):517-22. doi: 10.5664/jcsm.3700.

Hypercapnia is a key correlate of EEG activation and daytime sleepiness in hypercapnic sleep disordered breathing patients.

Hypercapnia is a key correlate of EEG activation and daytime sleepiness in hypercapnic SDB patients. The relationship between hypercapnia and sleepiness may be mediated by reduced **neuro-electrical brain activity** (Delta/Alpha ratio)

McSharry DG, et al . Respirology 2012; 17: 1119–1124.
Saaresranta T, et al. Respir Med 2005; 99: 856–863

COPD and insomnia
J Clin Med 2015;11(3):259-270

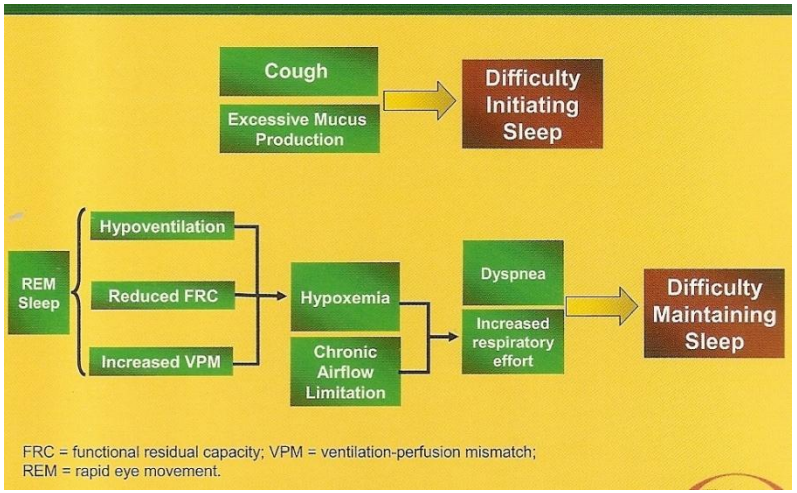


Table 1—Possible etiologies of insomnia in patients with COPD.

- Respiratory symptoms including cough, sputum production and dyspnea
- Nicotine use
- Nicotine withdrawal
- Increased work of breathing
- Hypoxia
- Increased Sympathetic Activity
- Comorbid anxiety and depression
- Comorbid sleep disorders including SDB and RLS
- Use of medications such as theophylline

COPD patients with insomnia:

- low health-related quality of life
- low self-reported sleep quality
- are more likely to suffer from daytime sleepiness.
- decreased productivity at work, absenteeism, and traffic accidents

The relationship between sleep disturbance and health status in patients with COPD

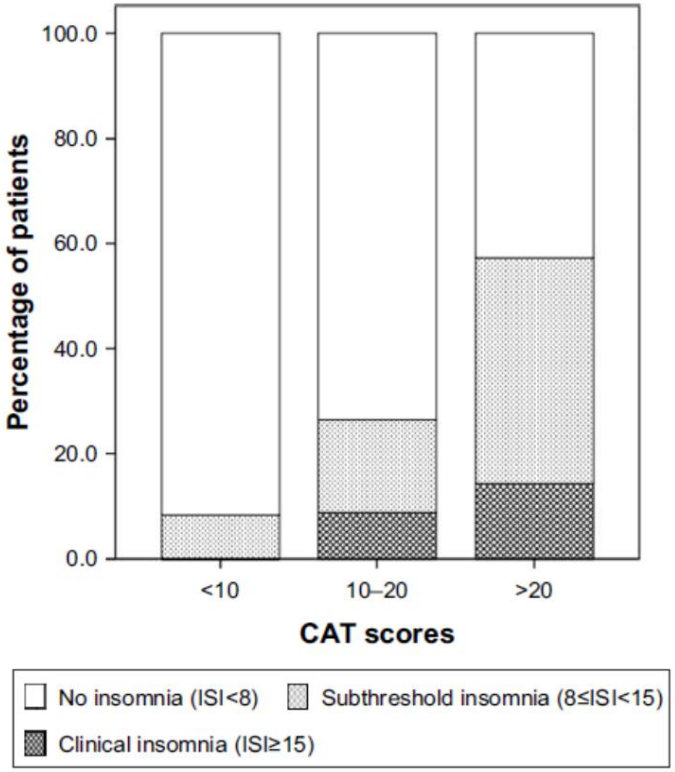
International Journal of COPD 2018:13

Introduction: The detection of insomnia in patients with COPD is assumed to be significantly lower than the actual prevalence. In this study, we investigated the prevalence of insomnia and the relationship between insomnia and health status in patients with COPD using two fairly simple and straightforward questionnaires: COPD assessment test (CAT) and insomnia severity index (ISI).

Patients and methods: A cross-sectional study was conducted using data from patients undergoing treatment for COPD at St Paul's Hospital, The Catholic University of Korea, between December 2015 and August 2016. Patients were classified into three groups according to the ISI score: a "clinical insomnia" group (ISI≥15), a "subthreshold insomnia" group (ISI 8–15), and a "non-insomnia" group (ISI<8). Clinical parameters including past medical history, pulmonary function tests, and questionnaire data were collected and analyzed.

Results: A total of 192 patients were recruited, of which 25.0% were found to have clinical insomnia (ISI≥8). Insomnia severity was related to all CAT component items except for cough, and patients with higher CAT scores generally had more severe insomnia. Logistic regression analysis revealed that CAT score was significantly associated with insomnia in these patients (odds ratio, 1.23; 95% CI, 1.13–1.34; $p<0.0001$). CAT score was also a significant predictor of insomnia (area under receiver operating characteristic curve, 0.779; $p<0.001$). The optimal predictive cutoff value was a CAT score >14, giving a sensitivity and specificity of 66.7% and 71.5%, respectively.

Conclusion: CAT score was closely related to insomnia severity in patients with COPD. The use of CAT scores to assess for the presence and severity of insomnia in these patients may allow for better detection and management and improve clinical practice.



REVIEW ARTICLES

JCSM
Journal of Clinical Sleep Medicine

pii: jc-00080-14
http://dx.doi.org/10.5664/jcsm.4540

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

Rohit Budhiraja, MD[1]; Tauseef A. Siddiqi, MD[2]; Stuart F. Quan, MD[2,3]

J Clin Sleep Med 2015;11(3):259–270.

CENTRAL SLEEP APNEA

There is a dearth of studies assessing prevalence of central sleep disordered breathing in patients with COPD. COPD is associated with several comorbidities or complications, which in turn can be associated with central sleep apnea or Cheyne-Stokes respiration. For example, patients with severe COPD can develop pulmonary hypertension and right ventricular dysfunction. One case series of 38 patients with pulmonary hypertension from different etiologies revealed Cheyne-Stokes respiration in 39% of the patients.[145] Similarly, COPD is frequently associated with left ventricle diastolic dysfunction[146] as well as systolic heart failure,[147] both conditions known to be associated with Cheyne-Stokes respiration.

RESTLESS LEGS SYNDROME

The prevalence of RLS is higher in persons with COPD than those without COPD.[153] One study showed significantly higher odds of incidence of RLS in those with self-reported obstructive airway disease than those without obstructive airway disease (OR = 2.8).[5]

While the etiology of RLS in COPD is yet to be clearly elucidated, hypoxemia and/or hypercapnia may contribute to the pathogenesis of RLS. Indeed, a higher prevalence of RLS has been reported in other pulmonary disorders including sarcoidosis and pulmonary hypertension. Hypoxia, through the hypoxia inducible factor-1 (HIF-1) pathway, may lead to an increase in tyrosine hydroxylase and vascular endothelial growth factor (VEGF). The former is a rate limiting enzyme in dopamine synthesis and is increased in RLS. VEGF expression is increased in the substantia nigra and in the anterior tibialis muscles of those suffering from RLS. Alterations in nigrostriatal and/or extrastriatal dopaminergic pathways may be seen in persons with RLS. Nicotine, the primary risk factor for COPD, exerts some effects through stimulation of dopaminergic pathways. Whether these are related, and could influence the association between COPD and RLS is unclear. Iron deficiency is likely causally related to RLS.[154] Low ferritin in some COPD patients may be responsible for RLS. Similarly, comorbid renal failure may underlie RLS in some patients. Several medications including antidepressants and dopamine antagonists can worsen restless legs syndrome symptoms.[155] Finally, some individuals may be genetically predisposed to develop RLS.[156]

Night-time dyspnoea in COPD patients

TABLE 1 Prevalence of night time dyspnoea according to different characteristics describing individuals with chronic obstructive pulmonary disease

	Prevalence of night-time dyspnoea	p-value
Wheezing		
No	2.1 [98/4691]	<0.001
Yes	9.8 [180/1835]	
Chronic mucus hypersecretion		
No	2.7 [145/5288]	<0.001
Yes	10.5 [135/1288]	
Peripheral oxygen saturation		
>92%	4.1 [265/6438]	0.002
≤92%	10.0 [14/140]	
mMRC score		
<2	2.1 [115/5392]	<0.001
≥2#	13.7 [168/1224]	
Troubled by breathlessness		
Not often	2.3 [139/5977]	<0.001
Often	23.7 [142/600]	
Exacerbations in previous year		
0	4.0 [257/6373]	<0.001
1	7.0 [8/114]	
≥2	14.0 [18/129]	
Treated with any inhaled medication		
No	3.6 [212/5956]	<0.001
Yes	10.8 [71/660]	
GOLD		
Grade¶		
1	3.0 [99/3301]	<0.001
2	4.9 [139/2845]	
3	8.9 [38/425]	
4	15.6 [7/45]	
Group+		
A	2.1 [108/5121]	<0.001
B	12.9 [120/930]	
C	2.6 [7/271]	
D	16.3 [48/294]	

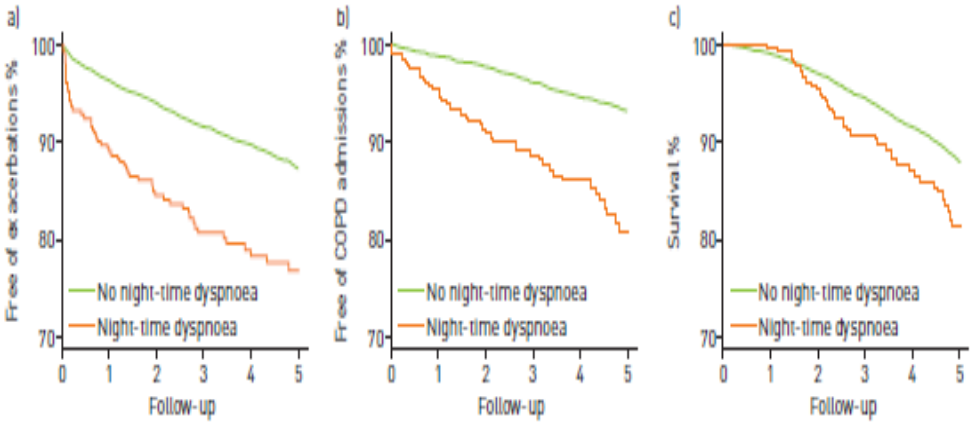


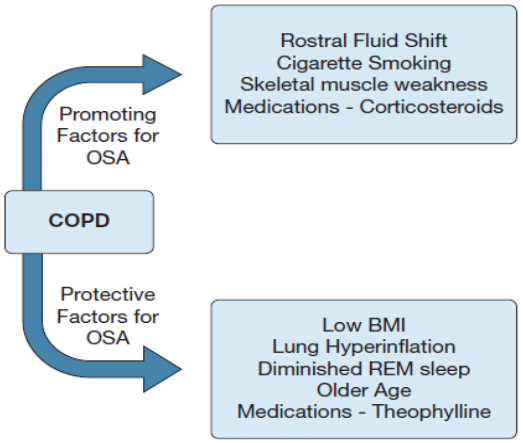
FIGURE 1 a) Exacerbations ($p<0.001$), b) hospital admissions due to chronic obstructive pulmonary disease (COPD) ($p<0.001$) and c) survival ($p=0.004$) shown as Kaplan–Meier curves according to absence or presence of night-time dyspnoea. Significance values are based on the log-rank test.

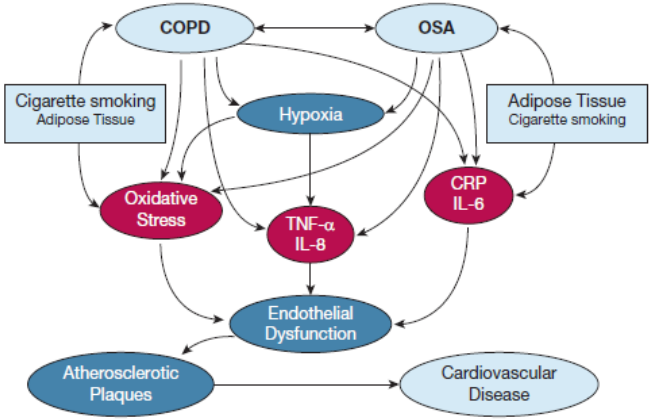
COPD-OSA Overlap Syndrome

- The concurrent presence of COPD and OSA in one individual is referred to as the “overlap syndrome”, a term first introduced by D.C. Flenley in 1985.
- The diagnosis is made by full, in-laboratory PSG performed on a patient with COPD who presents with sleep-related complaints. Prevalence ranged (in COPD population) from 8-55%
- The typical PSG features are recurrent episodes of apnoeas and/or hypopneas alternating with hyperpnea, arousals, and a variable degree of oxygen desaturations and/or hypoventilation (REM sleep).

Sleep Medicine Reviews 32 (2017) 58–68

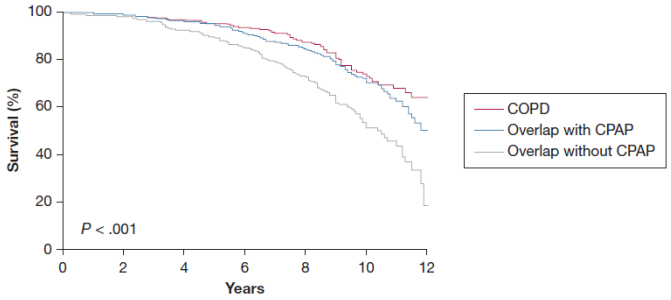
Overlap Syndrome

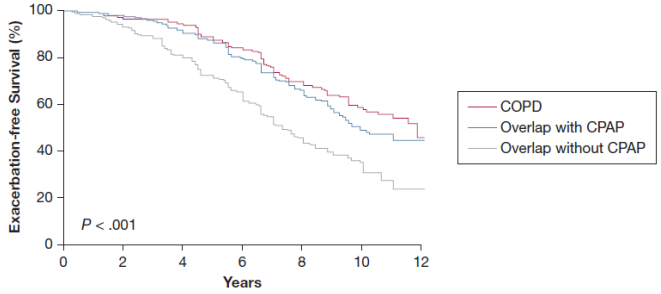




J Clin Med 2015;11(3):259-270

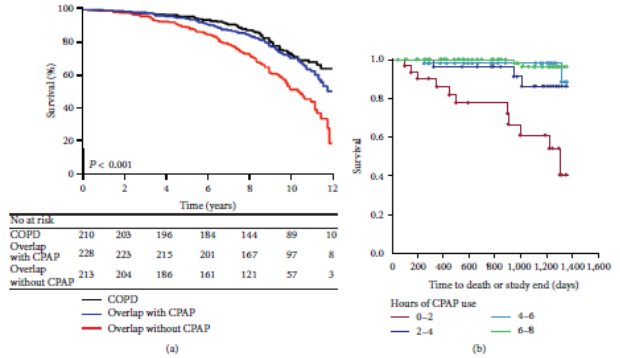
Expert Rev. Respir. Med. 8(1), 79–88 (2014)





CHEST 2017; 152(6):1318-1326

Canadian Respiratory Journal 3



Canadian Respiratory Journal
Volume 2016, Article ID 7947198, 5 pages

Characteristics of COPD pt with probability of SBD- Diagnosis

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

•Awake SaO2<95%, increased TST<90%

•Sleep complaints or symptoms suggestive of OSA

•Pts with mild COPD and evidence of pulmonary hypertension or daytime hypercapnia (borderline daytime hypercapnia with bicarbonate retension)

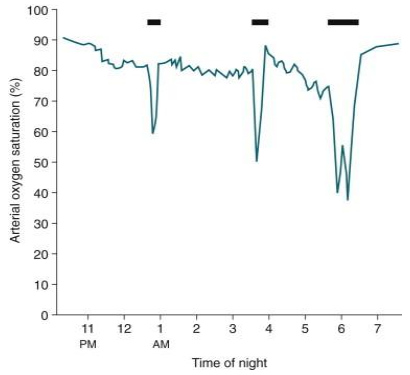
•More CV morbidity, poorer sleep quality, frequent COPD exacerbations and increased medical cost

•COPD pts who develop morning headaches when treated with nocturnal supplemental oxygen

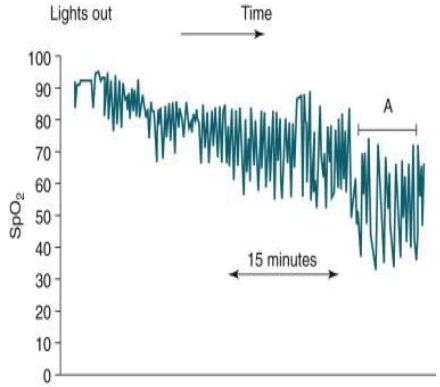
- Nocturnal oximetry (2 channels: heart rate and oximetry), however can't effectively differentiate nocturnal hypoxemia from COPD or OSA
- PSG with EtCO2: the current best diagnostic tool
- The role of unattended portable sleep study is unclear and more research is needed

Canadian Respiratory Journal
Volume 2016, Article ID 7947198, 5 pages

The typical pattern of nocturnal oxygen desaturation in COPD and overlap syndrome



COPD



Overlap syndrome

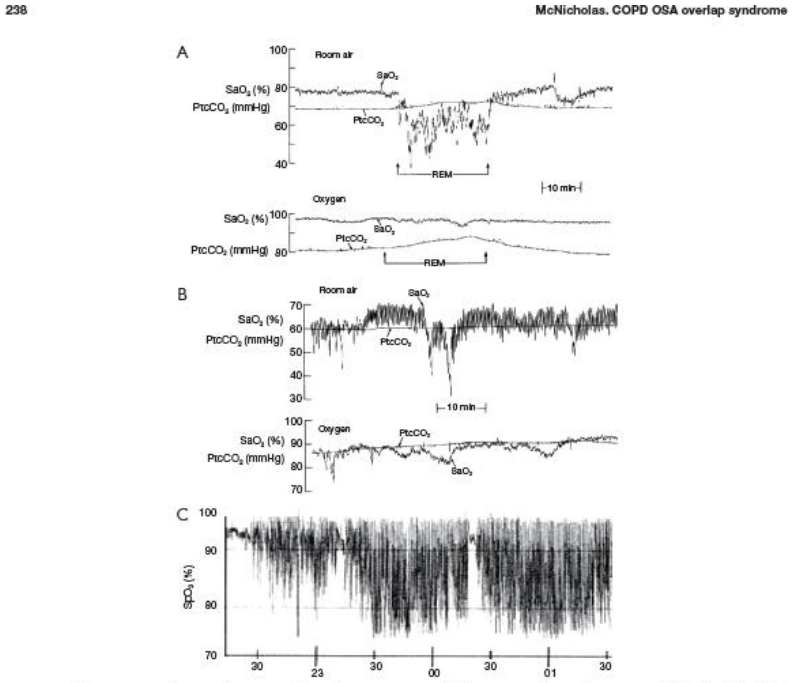


Figure 1 Different patterns of oxygen desaturation during sleep in patients with COPD (A), overlap syndrome (B) and OSA (C). SaO_2/SpO_2, oxygen saturation; $PtcCO_2$, transcutaneous carbon dioxide tension; REM, rapid-eye-movement; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnoea.

J Thorac Dis 2016;8(2):236-242

Berry RB: Sleep Medicine Pearls 2nd ed. Philadelphia: Hanley & Belfus, 2003

PSG patterns

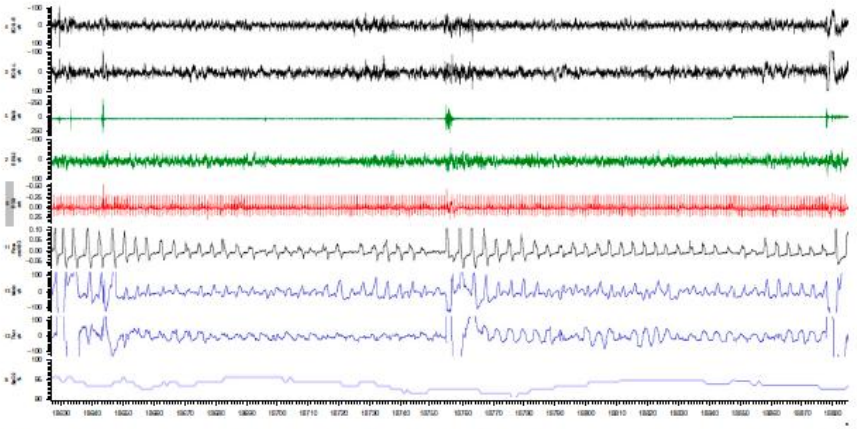


Figure 2. Prolonged respiratory events. A representative polysomnograph recording in a patient with sleep-disordered breathing and obstructive lung disease demonstrates how sustained desaturation due to prolonged hypoventilation would be counted as a single respiratory event.

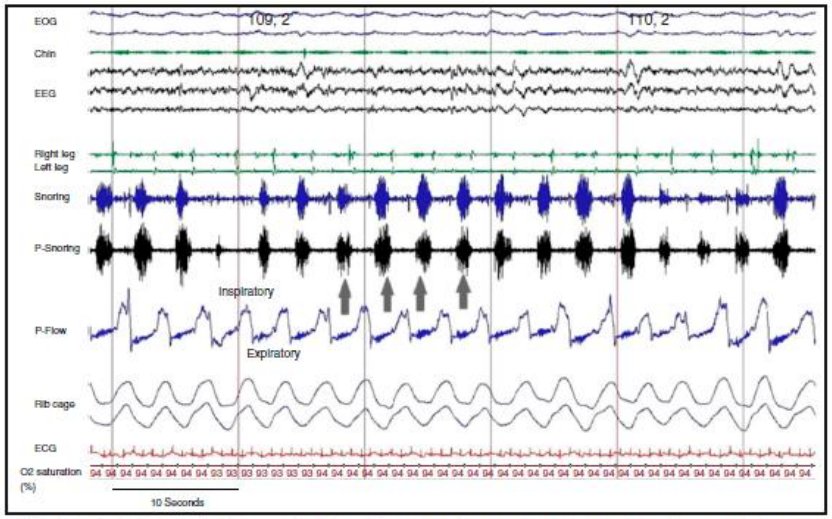


Figure 4. Expiratory flow limitation and expiratory snoring in chronic obstructive pulmonary disease. A representative polysomnograph recording during non-REM sleep in a patient with sleep-disordered breathing and obstructive lung disease. Arrows point to the expiratory flow limitation and expiratory snoring. Chin = chin electromyogram; EOG = electrooculogram; P-Flow = pressure flow; P-Snoring = snoring tracing obtained by pressure flow sensor; snoring = snoring tracing obtained by chin microphone (53).

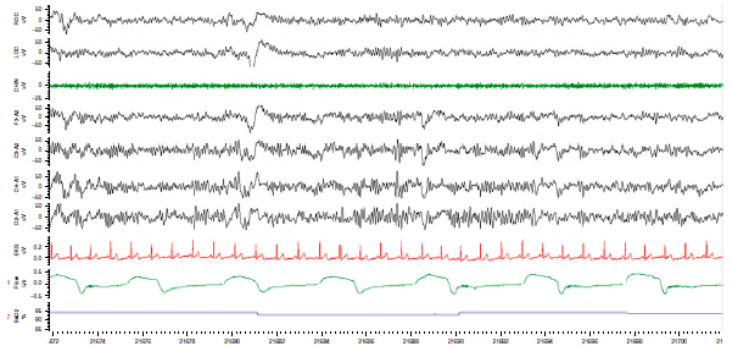
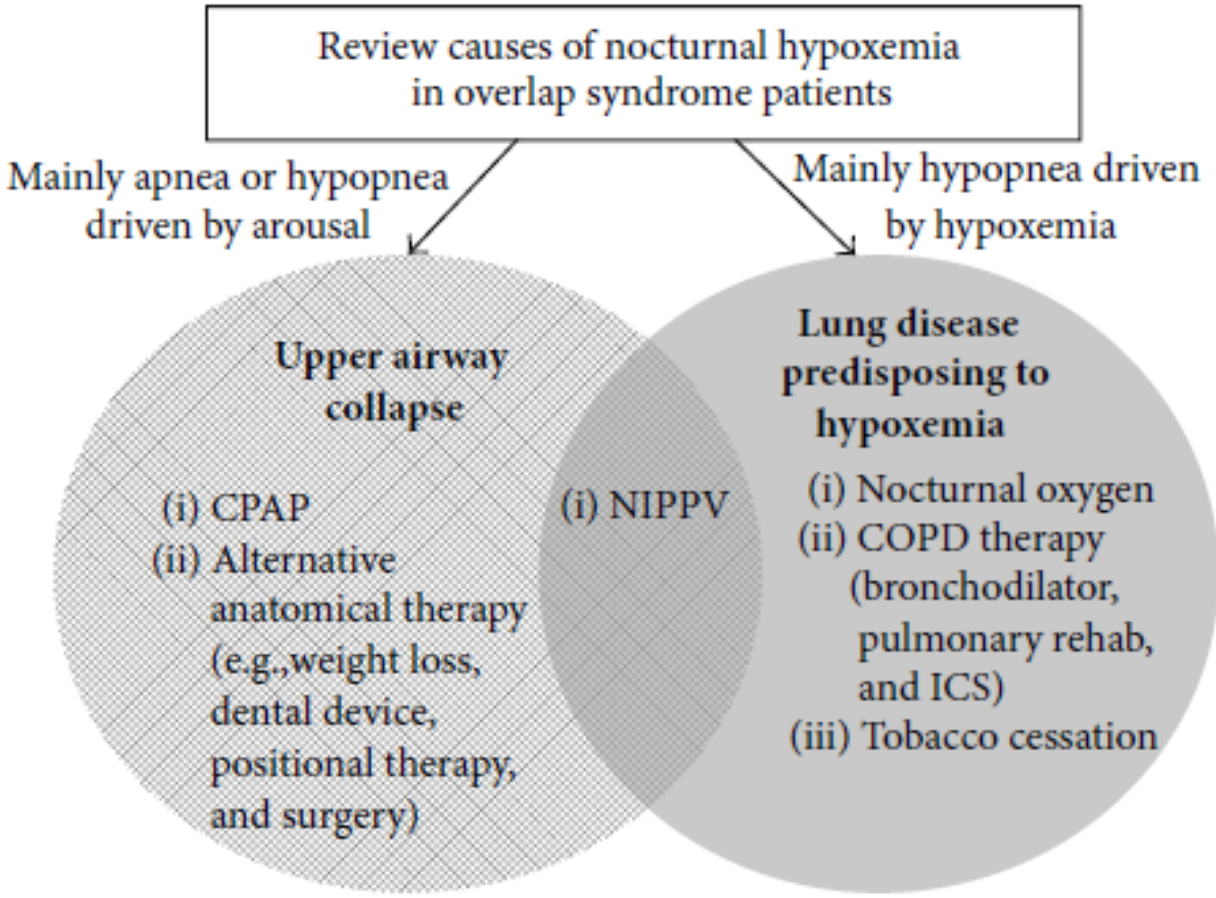


Figure 3. Alpha intrusion. A representative polysomnograph recording in a patient with sleep-disordered breathing and obstructive lung disease demonstrates an increase in alpha intrusion and illustrates how it can be difficult to detect hypopneas terminating in arousals from sleep.

Treatment options



Jen R, LiY, Owens RL, Malhotra A. Can Respir J. 2016;2016:7947198.

Pharmacologic therapy

- Bronchodilators
- Glucocorticosteroids
- Other pharmacologic treatments

LTOT in COPD

J Clin Med 2015;11(3):259-270
Fleetham J, Am Rev Respir Dis 1982; 126:429.-33

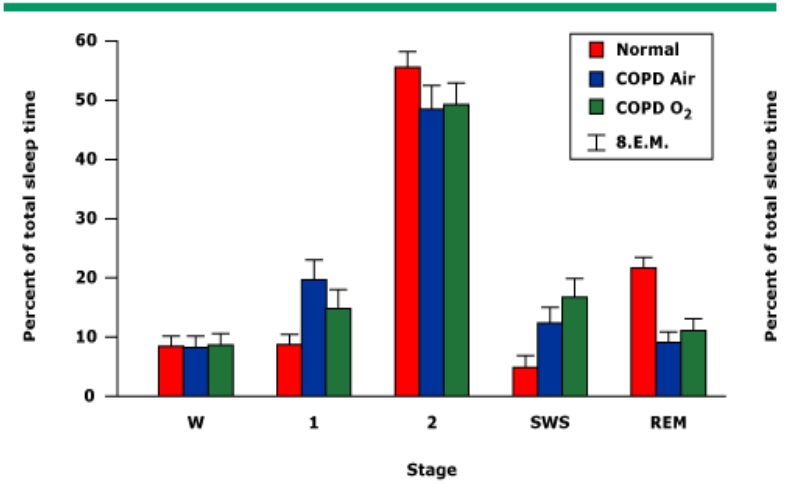
Table 2—Potential beneficial effects of oxygen on sleep and breathing in COPD.

- Decreases minute ventilation, preventing auto-PEEP
- Alleviates nocturnal hypoxemia-associated arousals
- Decreases pulmonary artery pressures
- Alleviates anxiety and depression
- Attenuates sympathetic activity

Lacasse YCIoHRC, Multi-Center Randomized Placebo-controlled Trial of Nocturnal Oxygen Therapy in Chronic Obstructive Pulmonary Disease. The International Nocturnal Oxygen (INOX) Trial, https://clinicaltrials.gov/ct2/show/record/https://clinicaltrials.gov/ct2/show/record/NCT01044628.

National Heart, Lung, and Blood Institute (NHLBI); Centers for Medicare and Medicaid Services, Effectiveness of Long-Term Oxygen Therapy in Treating People with Chronic Obstructive Pulmonary Disease, https://clinicaltrials.gov/ct2/show/NCT-00692198.

Sleep stages as a percentage of total sleep time in COPD



Global Strategy for Diagnosis, Management and Prevention of COPD
Manage Stable COPD: Pharmacologic Therapy
(Medications in each box are mentioned in alphabetical order, and therefore not necessarily in order of preference.)

Patient	Recommended First choice	Alternati	
A	**SAMA** prn or **SABA** prn	**LA** or **SABA** and **SAMA**	Theophylline
B	**LAMA** or **LABA**	**LAMA** and **LABA**	**SABA** and/or **SAMA** Theophylline
C	ICS + **LABA** or **LAMA**	**LAMA** and **LABA** or **LAMA** and PDE4-inh. or **LABA** and PDE4-inh.	**SABA** and/or **SAMA** Theophylline
D	ICS + **LABA** and/or **LAMA**	ICS + **LABA** and **LAMA** or ICS+**LABA** and PDE4-inh. or **LAMA** and **LABA** or **LAMA** and PDE4-inh.	Carbocysteine N-acetylcysteine **SABA** and/or **SAMA** Theophylline

Βρογχοδιαστολή: Θεμέλιος λίθος στην θεραπεία της ΧΑΠ

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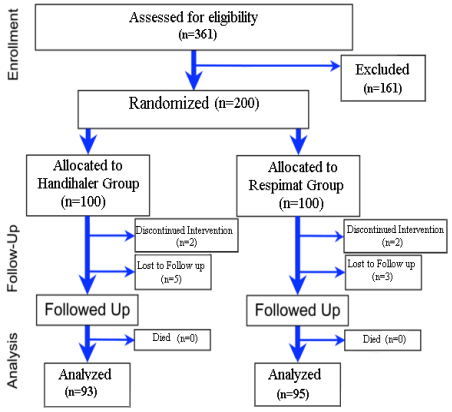
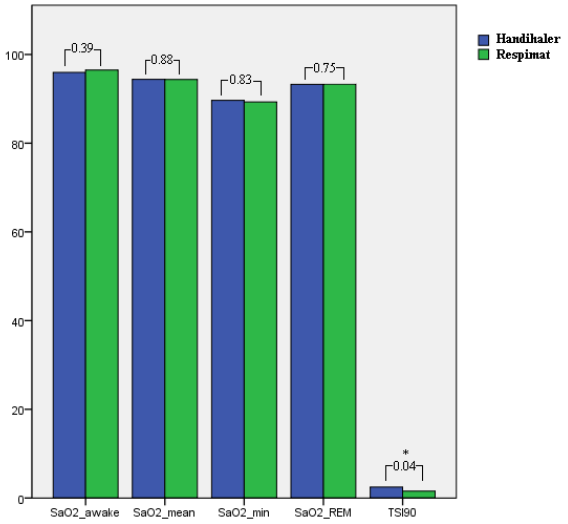
SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

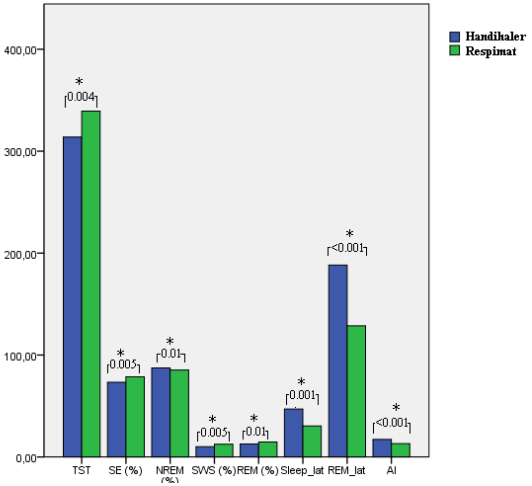
Tiotropium Respimat Soft Mist Inhaler versus HandiHaler to improve sleeping oxygen saturation and sleep quality in COPD

Izolde Bouloukaki[1] · Nikolaos Tzanakis[1] · Charalampos Mermigkis[1] · Katerina Giannadaki[1] · Violeta Moniaki[1] · Eleni Mauroudi[1] · Stylianos Michelakis[1] · Sophia E. Schiza[1]

- Randomized, parallel-group trial
- Patients with mild to moderate stable COPD
- Comparison of the effect of 6 months therapy of 2 devices on
  - sleeping oxygen saturation and
  - sleep quality in patients with COPD, after treatment initiation.







Bouloukaki I, et al. Sleep Breath. 2016 May;20:605-12

TABLE 11

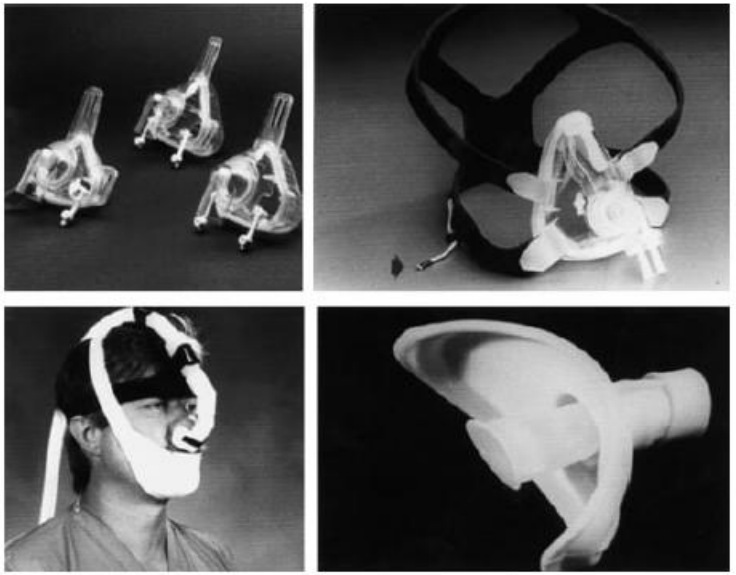
GOALS OF NONINVASIVE VENTILATION

Short-term (including acute)

1. Relieve symptoms
2. Reduce work of breathing
3. Improve or stabilize gas exchange
4. Optimize patient comfort
5. Good patient-ventilator synchrony
6. Minimize risk
7. Avoid intubation

Long-term

1. Improve sleep duration and quality
2. Maximize quality of life
3. Enhance functional status
4. Prolong survival



Mehta S et al. AJRCCM 2001

European Respiratory Society guidelines on long-term home non-invasive ventilation for management of COPD

Begum Ergan[1,23], Simon Oczkowski[2,3,23], Bram Rochwerg[2,3], Annalisa Carlucci[4], Michelle Chatwin[5], Enrico Clini[6], Mark Elliott[7], Jesus Gonzalez-Bermejo[8,9], Nicholas Hart[10,11], Manel Lujan[12], Jacek Nasilowski[13], Stefano Nava[14], Jean Louis Pepin[15], Lara Pisani[14], Jan Hendrik Storre[16,17], Peter Wijkstra[18], Thomy Tonia[19], Jeanette Boyd[20], Raffaele Scala[21] and Wolfram Windisch[22]

TABLE 1 Recommendations for PICO (target population-intervention-comparator-outcome) questions

Question	Recommendation
Should LTH-NIV be used in stable patients with COPD (as compared to not using NIV)?	The ERS task force suggests LTH-NIV be used for patients with chronic stable hypercapnic COPD (conditional recommendation, low certainty evidence).
Should LTH-NIV be used after an episode of acute hypercapnic respiratory failure in patients with COPD (as compared to not using NIV)?	The ERS task force suggests LTH-NIV be used in patients with COPD following a life-threatening episode of acute hypercapnic respiratory failure requiring acute NIV, if hypercapnia persists following the episode (conditional recommendation, low certainty evidence).
When using LTH-NIV in COPD patients, should NIV settings be titrated to normalise or at least cause a significant reduction in P_{aCO_2} (as compared to titrating not according to P_{aCO_2} levels)?	The ERS task force suggests titrating LTH-NIV to normalise or reduce P_{aCO_2} levels in patients with COPD (conditional recommendation, very low certainty evidence).
When using LTH-NIV in COPD patients, should we use fixed pressure modes (as compared to adaptive or auto-titrating pressure modes)?	The ERS task force suggests using fixed pressure support mode as first-choice ventilator mode in patients with COPD using LTH-NIV (conditional recommendation, very low certainty evidence).

Sleep Disordered Breathing in COPD

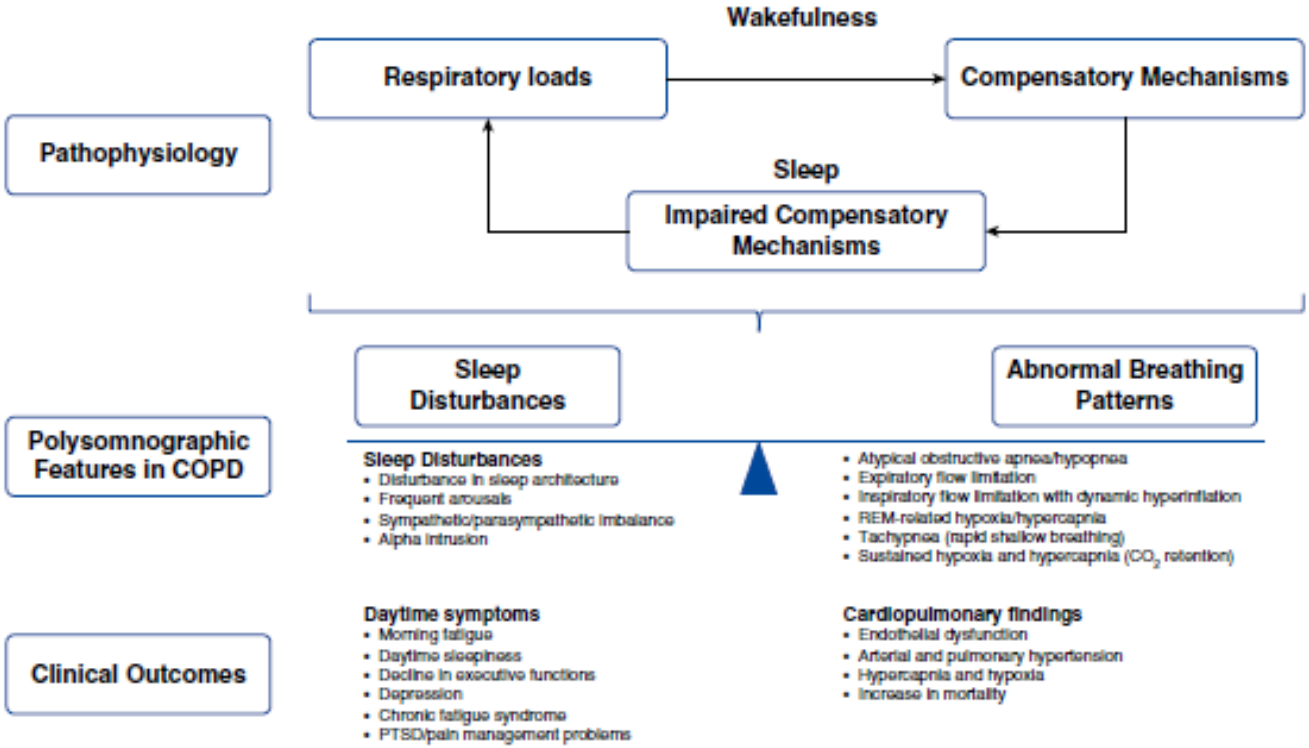


Figure 5. Sleep-disordered breathing in chronic obstructive pulmonary disease (COPD). PTSD = post-traumatic stress disorder.

PhD:
Επίδραση της θεραπείας με χορήγηση θετικών πιέσεων αέρα στους ανώτερους αεραγωγούς (PAP) στη νοσηρότητα και θνητότητα ασθενών με σύνδρομο αποφρακτικών απνοιών στον ύπνο και χρόνια αποφρακτική πνευμονοπάθεια (Σύνδρομο επικάλυψης)

Υποψήφιος διδάκτορας: Μιχάλης Φαναρίδης

Επιβλέπουσα: Αν. Καθηγήτρια Σοφία Σχίζα
Συν-επιβλέποντες: Καθηγητής Νίκος Τζανάκης
Αν. Καθηγητής Πασχάλης Στειρόπουλος

Σας ευχαριστώ για την προσοχή σας!!!!