ERS Annual Congress Barcelona
7 - 11 September 2013

Postgraduate Course 13
Respiratory complications of obese patients

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Saturday, 7 September 2013
14:00 - 17:30
Room: 3.6
Postgraduate Course 13
Respiratory complications of obese patients

Aims: Obesity is considered the 21 century epidemic and its respiratory complications are growing in today’s clinical practice. Research about obesity and related diseases is rapidly increasing. The aim of this postgraduate course is to provide respiratory physicians with updated information on the pathophysiology and clinical consequences of obesity in patients with respiratory problems. Participants will increase their knowledge and awareness about some clinical aspects typical of obese patients. Specifically, besides classical clinical situations such as the obesity-hypoventilation syndrome (OHS), the association of obesity and COPD will be addressed, as well as the growing problem of post-operative respiratory complications in obese patients. Finally, treatment of obese asthmatic patients will be discussed.

HERMES LINKS ADULT: B.1 Airway diseases, B.19 Sleep-related disorders, E.1 Treatment modalities and prevention measures.

Target audience: Pulmonologists, pathologists, respiratory physicians, clinical researchers, allergologists, research fellows, otolaryngologist, basic scientists, trainees.

Chairs: J. Montserrat (Barcelona, Spain), A. Ten Brinke (Molenend, Netherlands)

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COURSE PROGRAMME

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Complications of obesity in COPD patients

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Aims
Getting insights in the prevalence of obesity and the pathophysiological changes related to obesity in COPD, the role of obesity in phenotyping of COPD patients. Getting insights into adipokine metabolism in relation to obesity and the possible effects of adipokines in the pathophysiology of COPD.

Summary
Obesity is a major cause of worldwide morbidity and mortality. The prevalence of obesity in COPD varies across studies, probably as a result of differences in genetic and COPD specific risk factors for obesity. Obesity has profound impact on the respiratory mechanics in COPD patients and determines experienced symptomatology of the patient. Obesity is an important determinant of systemic inflammation and has been recognized as an important characteristic in certain COPD phenotypes. Intriguing is the role of adipokines (leptin, adiponectin) in the link between adipose tissue and the respiratory system.

References

Evaluation
1. Obesity has important effects on respiratory mechanics. One of the following statements is correct:
   a. Obesity increases ERV
   b. Obesity decreases TLC
   c. Obesity decreases FRC.

2. Obesity has important effects on exercise capacity. One of the following statements is correct:
   a. Obese patients do not experience greater exercise limitation than normal weight patients during peak cycle ergometry.
   b. Operating lung volumes are not modified by obesity in COPD.
c. Six minute walk is unaffected by obesity in COPD.

3. Systemic inflammation is a characteristic finding in COPD. One of the following statements is correct:
   a. Systemic inflammation in COPD is present in all COPD patients.
   b. Systemic inflammation in COPD is characterised by raised IL-8.
   c. Systemic inflammation in COPD is characterised by raised CRP and fibrinogen.

   Please find all correct answers at the back of your handout materials
Complications of obesity in the COPD patient

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CIRO+, center of expertise for chronic organ failure
The Netherlands

‘Globesity’

Obesity (BMI > 30 kg·m⁻²) is a preventable complex multifactorial chronic condition that develops from an interaction of genotype and the environment.

The worldwide prevalence of obesity has doubled since 1980, resulting in an estimated number of 500 million obese adults around the world in 2008.

Obesity is a major cause of worldwide morbidity and mortality

WHO, Global Database on BMI, 2013

Prevalence of obesity in COPD

The prevalence of obesity in COPD varies across studies, probably as a result of differences in general and COPD specific risk factors for obesity.

Prevalence of obesity in the Burden of Obstructive Lung Disease (BOLD) initiative (n=13,774)

Both in normal subjects as well as COPD, lower prevalence of obesity was observed in smokers. COPD subjects were less frequently obese.

Vanfleteren et al., in preparation

Lung function in obesity

Obesity
- Decreased lung compliance
- Decreased FRC and ERV, preserved TLC and VC

Impact on symptoms, lung function and exercise performance in COPD?

Franssen et al., Thorax 2008
Gifford et al., Chest 2010

Combined effects of obesity and COPD: lung function at rest

O'Donnell et al., Chest 2011
**COPD and obesity: symptoms and health status**

**Dyspnea**

- **Health status**

**Exercise capacity in normal weight and obese COPD patients**

Obese COPD patients do not experience greater exercise limitation and dyspnea than normal weight patients during peak cycle ergometry.

**Operating lung volumes during cycling exercise in normal weight and obese COPD**

**Cecere et al., COPD 2011**

**Ora et al., Am J Respir Crit Care Med 2009**
In contrast to cycle ergometry, six minute walking distance is shorter in obese COPD patients compared with non-obese patients. Bautista et al., Respir Med 2011

However, walk-work and physiologic responses to walking were comparable in both groups.

Obesity and osteoporosis in COPD
Overweight and obese COPD patients have a decreased risk of osteoporosis. Increased mechanical loading and secretion of bone active hormones (leptin, insulin) may contribute. Graat-Verboom et al., Bone 2012

Combined effects of obesity and COPD: prognosis
Schols et al., Am J Respir Crit Care Med 1998
Combined effects of obesity and COPD: obesity paradox

Fat mass contributes to systemic inflammation in COPD

Management of obesity in COPD

WHY?

HOW?

VLCD?

Activity?

Surgery?

Drugs?
Multidimensional treatment of adult obesity

Pharmacotherapy
Dietary therapy
Surgery
Behavioral modification
(ilmişgging smoking cessation)
Physical activity

Role for pulmonary rehabilitation?


The impact of obesity on response to pulmonary rehabilitation in COPD

Obesity and overweight do not influence the magnitude of improvement after pulmonary rehabilitation

Sava et al., BMC Pulm Med 2010
Sleep Apnea and the obesity-hypoventilation syndrome

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Summary

Definition
Sleep apnea syndrome is a disorder characterized by excessive sleepiness, cognitive-behavioral, respiratory, cardiac, metabolic and inflammatory alterations secondary to repeated episodes of upper airway obstruction during sleep [1]. Since these episodes are measured by the apnea hypopnea index (AHI), previous definitions included an abnormal AHI (i.e. ≥5) associated with symptoms related to the disease and unexplained by other causes. However, patients with high levels of AHI (i.e. >40) can have no symptoms or consequences, while pauci-symptomatic patients can have related cardiovascular events. Nowadays, therefore, most of the national guideline recommends considered sleep apnea and hypopnea syndrome as solely an abnormal AHI [2], generally, ≥5 [1-7].

Epidemiology
Obstructive sleep apnea (OSA) is a very frequent disease, with a prevalence of almost 25% in the adult population [8]. Its consequences are a reduction in the quality of life [9], an increase in cardiovascular events and mortality [10,11] and traffic accidents [12,13]. The most important risk factors are age, sex (male) and body mass index. The prevalence in elderly people is three times that of middle-aged subjects, and the prevalence in men is 2-3 times that in women, although the levels in women become more similar after the menopause. Other variables that influence the appearance of OSA or its severity are alcohol, tobacco, sedatives, hypnotics and barbiturates, and the supine decubitus position. Other potential implications are genetics, family and ethnic group. The severity of the disease has arbitrarily been classified as: mild (AHI: 5-14.9); moderate (AHI: 15-29.9) and severe (AHI > 30) [14].

Pathophysiology
The mechanisms that lead to collapse of the upper airway are not totally clear but they probably correspond to the interaction between anatomic and functional factors. The pharynx is the most collapsible segment of the upper airway; it can close as a result of an imbalance between forces that tend to close it and others that tend to keep it open. Deficiencies in the reflexes, respiratory center or the pharynx muscles themselves (which could have a genetic origin), as well as anatomic predisposition, can favor the forces that tend to close the pharynx. The occurrence of central or obstructive events seems to be critically dependent on the respiratory rhythm of PaCO2 variations in the former events and on the local (pharynx) imbalance between dilator muscles and compliance in the latter. Both central and obstructive events can occur repetitively. This cyclical behavior essentially depends on the arousal sensitivity and the hyperventilatory response, resulting in hypocapnia [15].

Clinical Features
The symptoms related to OSA can be a consequence of two physiopathological factors, intermittent hypoxia (secondary to apneas and hypopneas) and sleep fragmentation (secondary to arousals). The symptoms and signs can appear during the night or during the day. Comprehensive clinical evaluation is important because it makes it possible to classify patients as having a low, intermediate or high pretest clinical probability of sleep apnea. This is important for the subsequent selection of the diagnostic methods.
The cardinal symptoms are snoring, observed apneas and sleepiness as identified by subjective or objective measurements. The more common subjective evaluation is the Epworth sleepiness scale [16] (Figure 1), where a score equal to or greater than 12 points (out of 24) indicates pathological sleepiness. Objective methods include the multiple sleep latency test (MSLT), the maintenance of wakefulness test (MWT), the Osler test and the motor skills wakefulness test. Some diseases have a high risk of being associated with OSA, so any related symptoms should be evaluated (Figure 2), by a sleep study if necessary.

Cardiovascular consequences
Apneas and hyponeas cause intermittent hypoxia, arousals and significant intrathoracic negative pressure (Figure 3), which produce, as intermediate mechanisms, sympathetic activation [17], hypercoagulability, inflammation, oxidative stress, endothelial dysfunction [18], metabolic deregulation (insulin resistance) [19] and systolic and diastolic dysfunction [20]. The cardiovascular consequences are systemic hypertension, arrhythmias, myocardial infarction, heart failure, stroke and sudden death.

Hypertension
Some meta-analyses have demonstrated a blood pressure reduction of close to 2 mmHg in systolic and diastolic pressure in patients with sleep apnea [21]. This reduction seems more relevant in patients with higher baseline blood pressure, higher BMI, more severe OSA and adequate CPAP compliance [22]. A reduction of only 2 mmHg represents a 17% decrease in the prevalence of hypertension, a 16% reduction in the risk of coronary heart disease and a 15% reduction in the risk of stroke and transient ischemic attack [23]. Sleepiness was believed to be a necessary factor for achieving blood pressure reduction with CPAP treatment [24]. A recent study has, however, shown similar blood pressure reduction in paucisymptomatic patients if they present adequate CPAP compliance [25]. Unpublished data from a large RCT in Spain revealed a reduction of 5 mmHg in the mean blood pressure of patients with refractory hypertension and OSA. Another published Spanish study that included 340 patients with “novo” hypertension and OSA has showed significant reduction in systolic and diastolic (nocturnal and daytime) pressure [26]. Despite these important results, CPAP should not be considered an antihypertensive treatment: one study has demonstrated that the antihypertensive effect of Valsartran is close to 8 times that of CPAP [27].

In summary, RCTs have shown that CPAP reduced blood pressure in OSAS patients, that CPAP could play a role in the management of hypertension, as well as in patients with resistant hypertension, and that the effect of CPAP on blood pressure is directly related to treatment compliance.

Cardiovascular mortality
Several observational studies have shown an increased risk of cardiovascular mortality in severe OSA patients untreated with CPAP (especially men) [28]. Recent observational studies performed on women [29] and elderly patients [30] have shown similar results. So, although observational studies show a high risk of cardiovascular mortality, there is currently insufficient evidence to recommend CPAP treatment for mortality risk prevention. Large multicenter RCTs are therefore necessary.

Traffic accidents
The mean risk ratio in professional or unprofessional drivers with sleep apnea is 3:1 [12, 13,31]. Accidents have been related to AHI [32] but not clearly to sleepiness [33], although some studies do suggest a closer relationship with sleepiness when driving [13]. RCTs performed after CPAP treatment suggest a reduction in the risk of traffic accidents [34].

Diagnostic methods
Attended in-hospital PSG is the gold standard method for the diagnosis of sleep apnea and other sleep disorders [35]. This involves the continuous recording of the neurophysiological, cardiac and respiratory variables described in Figure 4 for at least 6.5 hours. To be considered valid, a PSG
must have a sleep time of at least 3 hours. It is technically complex, time-consuming and expensive, and it is therefore unable to satisfy the high demand for diagnostic sleep studies. Home sleep studies with portable monitoring devices have been proposed to reduce costs and facilitate the diagnostic process [36,37]. Portable monitoring devices have been grouped into four categories, basically depending on the number of recorded channels [38] (Figure 4).

The type-3 method of portable monitoring, known as respiratory polygraphy (RP), includes nasal pressure as surrogated flow: it is recommended by the American Academy of Sleep Medicine [37] as a diagnostic alternative to PSG. Furthermore, the largest validation study plus cost analysis to date in patients with an intermediate-to-high clinical probability of sleep apnea showed that the total cost of home RP was half that of PSG for the same level of diagnostic efficacy when patients take the device home and the raw data file is telematically transmitted from home to hospital [39]. The therapeutic decision-making procedure is, however, not the same as the diagnostic process, as it involves the recommendation of CPAP (continuous positive airway pressure) or other treatments. A study has explored the efficacy of the therapeutic decision by home PR in comparison with PSG in the aforementioned cohort of patients in whom home RP diagnosis proved less costly than PSG. Agreement in the therapeutic decisions taken via home RP or PSG was acceptable only for severe cases of sleep apnea (AHI>30) [40]. Finally, another paper from the same cohort of patients studied the cost, for the same level of diagnosis and therapeutic decision efficacy (overall process), of various different strategies: a) PSG for the entire sample; b) home RP for the total sample; and c) home RP for the more symptomatic patients (high probability of being treated with CPAP) and PSG for the rest of patients. The cost of both home RP approaches was 20% lower in comparison with PSG. Another study that included patients with a high clinical probability of OSA has also demonstrated similar efficacy in patients managed (from diagnosis to treatment) by home RP and PSG [41]. Consequently, the method used to manage OSA patients by one would depend on the pretest clinical probability of the disease. Figure 5 summarizes this process: PSG would be reserved for no OSA disorders and for patients with low and intermediate clinical probability of OSA. Home RP could also be used for establishing the diagnosis in patients with an intermediate clinical probability but therapeutic decision should be considered only for patients with AHI>30; other patients should be referred to PSG. In patients with a high clinical probability of OSA, home RP can be used, although patients without a diagnosis (i.e. AHI <10) require a PSG.

**Choice of treatment**

The objectives of treatment are to minimize the symptoms and decrease the risks of cardiovascular events and traffic accidents. Various approaches can be used but CPAP is the treatment of choice for most patients. Figure 6 shows an algorithm for choice of treatment according to the relevance of the clinical symptoms or consequences and the AHI level. CPAP should be considered for patients with an AHI>30 and for those with an AHI of 5-30, as well as relevant clinical symptoms or associated morbidity.

Sleep hygiene measures such as the maintenance of adequate sleep habits, abstinence from alcohol and tobacco, avoidance of drugs that depress the respiratory center and adoption of the decubitus supine position to sleep must always be recommended, along with weight reduction in patients with a BMI>25. In patients with a BMI>40 bariatric surgery can be considered. Mandibular advancement devices are effective in patients with mild or moderate OSA with low BMI and significant desaturations [42]. Mandibular advancement devices can also be recommended as a second treatment line for patients who do not tolerate CPAP treatment. In comparison with CPAP, mandibular advancement devices show greater efficacy in reducing the AHI, as well as being better tolerated than CPAP treatment, while the improvement in clinical symptoms seems similar [43].

**Surgical treatment**

Oropharyngeal surgery: the selection of patients is similar to that of mandibular advancement devices. Over 50% of treated patients would benefit from it. Tongue base reduction surgery: the success rate ranges from 40-50% in treated patients. The selection of patients seems similar to that of oropharyngeal surgery.
Multilevel surgery: this is a very invasive surgical technique that should be preceded by a very precise anatomical study. It could be effective for an experienced surgical group team [44] but it is not widely used and the results from highly specialized teams cannot be extrapolated to others.

Obesity hypoventilation syndrome

**Definition**

Obesity-hypoventilation syndrome (OHS) is defined as the simultaneous occurrence of diurnal hypoventilation (PaCO2>45), obesity (BMI>30) and respiratory sleep disorders [45] if it is possible to exclude other causes of alveolar hypoventilation, such as severe obstructive or restrictive pulmonary disease, significant kyphoscoliosis, severe hypothyroidism, neuromuscular diseases and other central hypoventilation syndromes. Hypoventilation can be the only respiratory sleep disorder involved, although most patients also suffer from OSA (90%) [46,47].

**Epidemiology**

There are no epidemiological studies on the prevalence of OHS in the general population, although this has been estimated as being 0.15-0.3%. The prevalence in patients with suspected sleep apnea varies from one study to another, within a range of 10-30%, according to the methods used, country, cut-off of sleep apnea diagnosis [48]. In subjects with unknown OHS the prevalence of OHS ranges from 9 to 14% [49], while it is 7 to 22% in subjects referred to bariatric surgery [49]. It is not totally clear whether OHS is more common in men or women, although when several series of patients are considered together it seems more frequent in men (66%) [50].

**Pathophysiology**

Several mechanisms have been proposed to explain daytime hypercapnia in OHS, such as abnormal respiratory mechanisms (including respiratory muscle dysfunction), abnormal central responses to hypercapnia and hypoxia, neurohormonal dysfunction (leptin resistance) and sleep disordered breathing. Figure 7 shows the potential interaction between mechanisms. Sleep disorders produce a repetitive increase in nocturnal hypercapnia with progressive CO2 accumulation [51], which leads to a daytime increase in bicarbonate and a subsequent blunting of the PaCO2 drive to the respiratory center. Central leptin resistance can increase sleep disorders, as well as leading to central hypoventilation. Muscular fatigue can increase both daytime hypercapnia and nocturnal hypoventilation. CPAP mainly acts on obstructive events while NIV probably acts on most of the mechanisms implicated in daytime hypercapnia in OHS.

**Clinical Features**

OHS patient’s present obesity, a plethoric complexion, dyspnea, cyanosis and evidence of right heart failure, including peripheral edema [45]. Given that sleep apnea is normally present in OHS, loud snoring, nocturnal choking episodes with witnessed apneas, excessive daytime sleepiness, morning headaches and tiredness can be found. In comparison with obese subjects with eucapnia, OHS patients have more severe OSA, impaired respiratory mechanics, blunted central respiratory drive and increased incidence of pulmonary hypertension (review de anesthesia).

**Diagnosis**

OHS must be considered in obese patients (BMI>30) with daytime hypercapnia (PaCO2>45 mmHg) without any presence of other diseases that potentially cause hypercapnia. Pulmonary function tests can be normal but more often they show a mild-to-moderate restrictive disorder associated with the mechanical alterations of obesity. PSG is the method of choice for evaluating sleep disorders.

**Prognosis**

Patients with OHS have severe OSA and metabolic syndrome, as well as obesity itself, and these can result in cardiovascular mobility and mortality [52-56]. One retrospective study on
untreated patients found a mortality rate of 46% after 50 months of follow-up [47]. In another study, the mortality rate in eucapnic obese subjects was 9% and 23% in OHS 18 months after hospital discharge [57].

**Treatment**

**Weight reduction**

This is believed to be the ideal treatment for OHS. Respiratory insufficiency, pulmonary hypertension and sleep disorders [58] can be reversed if patients achieve a normal weight, although only a few maintain a significant weight reduction for a long period. Although bariatric surgery has been tested as an alternative treatment for OSA patients with extreme obesity, there are still some doubts about the benefit of this kind of therapy [59]. Less data are available in the case of OHS [60,6], especially as regards the long-term consequences. Moreover, bariatric surgery can be an alternative for only a minority of OHS patients due to the morbidity and mortality inherent in the surgical procedure itself for this type of patients [62].

**Ventilatory support**

NIV consists of the application of intermittent positive pressure ventilation, normally with bilevel positive pressure, using nasal or naso-oral masks. NIV can improve nocturnal hypercapnia by increasing alveolar ventilation, preventing obstructive events, improving leptin action (or preventing the resulting central hypoventilation) and providing more efficient direct muscular repose. Several series of cases and one RCT on 37 patients with mild hypercapnia [63] have shown improvements in the clinical picture, arterial blood gases and sleep disorders with this treatment [64-66]. A reduction in days of hospital admission has been observed in longitudinal studies [66,67]. Although no RCTs have been undertaken to assess whether NIV decreases mortality, this was the case in a series of patients treated with NIV, compared with other studies in which patients were not treated or refused treatment [68,69].

CPAP prevents obstructive events in patients with OHS but the PaCO2 is not normalized in all patients. Only one RCT has evaluated the clinical, PaCO2 and polysomnographic improvements in CPAP vs. NIV in 36 OHS patients selected for their favorable response to an initial night of CPAP treatment [70]. Similar results were observed in both groups but more RCTs (covering days in hospital and mortality) are required in non-selected patients to demonstrate which treatment is superior to the other in both the short and long term. Until more data are available a therapeutic proposal as presented in Figure 8 could be used.

**Oxygen therapy**

The nocturnal PaCO2 increased when a group of obese patients with nocturnal hypoventilation was treated with oxygen therapy [65] and this was not the case when the same patients were treated with NIV. Even in wakefulness and under stable conditions, OHS patients presented increased PaCO2 when treated with 100% oxygen concentration [71]. However, no RCT to date has assessed the benefits of long-term oxygen therapy in OHS, or of oxygen therapy together with weight loss. Although oxygen is frequently added to CPAP (40%) [72] or NIV, there are no studies evaluating its potential benefits.

**References**


**Evaluation**

1. What is true with regard to treatment with CPAP?
   a. Reduction of blood pressure is about 10 mmHg
   b. In general, patients with higher AHI have a similar decrease in blood pressure as for patients with low IAH.
c. BMI does not influence blood pressure lowering

d. The benefit depends upon compliance with CPAP.

2. What is false about how acts noninvasive ventilation?
   a. Unloading the respiratory muscles decreasing its chronic fatigue
   b. During sleep decreases or prevents alveolar hypoventilation (especially in the REM period) but not obstructive events.
   c. Prevents the elevation of PaCO2 and bicarbonate which cause a "blunting" of the respiratory center and hypercapnia.

3. Which treatment is believed to be the least effective for obesity hypoventilation syndrome?
   a. Weight loss by diet.
   b. Noninvasive intermittent mechanical ventilation
   c. CPAP.
   d. Medroxyprogesterone.

4. How is the diagnosis of obesity hypoventilation syndrome performed?
   a. Patients with sleep apnea and daytime hypercapnia regardless the presence of obesity and sleep apnea degrees.
   b. Patients with obesity (BMI>30), daytime hypercapnia (PCO2>45 mmHg) and sleep disorders when other diseases potentially causing hypercapnia have been excluded.
   c. Patients with obesity (BMI>30), daytime hypercapnia (PCO2>45 mmHg) and sleep apnea (AHI>30) without be necessary to consider other potentiely causes of daytime hypercapnia.
   d. Patients with obesity (BMI>30), severe sleep apnea (AHI>50) and nocturnal hypoventilation without daytime hypercapnia.

Please find all correct answers at the back of your handout materials
Figure 1

EPWORTH SLEEPINESS SCALE

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would affect you. Use the following scale to circle the most appropriate number for each situation:

0 = would never doze or fall asleep
1 = slight chance of dozing or falling asleep
2 = moderate chance of dozing or falling asleep
3 = high chance of dozing or falling asleep

<table>
<thead>
<tr>
<th>Situations</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 1 2 3</td>
<td></td>
</tr>
</tbody>
</table>

1. Sitting and reading
2. Watching TV
3. Sitting, inactive in a public place (e.g. a theater, a meeting, or a park)
4. As a passenger in a car for an hour without a break
5. Lying down to rest in the afternoon when circumstance permit
6. Sitting and talking to someone
7. Sitting quietly after a lunch without alcohol
8. In a car, while stopped for a few minutes in traffic

Figure 2

PATIENTS WITH HIGH RISK OF SLEEP APNEA IN WHOM RELATED SYMPTOMS SHOULD BE EVALUATED

Obesity (BMI > 35)
Cardiac insufficiency
Atrial fibrillation
Refractory hypertension
Type 2 diabetes mellitus
Nocturnal arrhythmias
Cerebrovascular accidents
Pulmonary hypertension
Individual with high risk of accidents
Pre-operative bariatric surgery
Chronic respiratory diseases with greater gasometric deterioration than expected
Figure 3

**OSA AND CARDIOVASCULAR DISEASE**

**FEATURES**
- HIPOXEMIA
- HIPERCAPNIA
- REDOXIGENATION
- INTRATORACIC PRESSURE CHANGES
- MICROAROUSALS

**INTERMEDIATE MECHANISMS**
- SYMPATHETIC ACTIVATION
- ENDOTHELIAL DISFUNCTION
- OXIDATIVE STRESS
- INFLAMATION
- HYPERCOAGULABILITY
- METABOLIC DYSREGULATION

**CARDIOVASCULAR CONSEQUENCES**
- SYSTEMIC HYPERTENSION
- ARTERIOSCLEROSIS
- ARRHYTHMIA
- MYOCARDIAL ISCHEMIA
- STROKE
- HEART FAILURE

Figure 4

**SLEEP STUDY METHODS**

<table>
<thead>
<tr>
<th>TYPE OF SLEEP STUDY (return example: PSG)</th>
<th>TYPE 1</th>
<th>TYPE 2</th>
<th>TYPE 3</th>
<th>TYPE 4</th>
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<tbody>
<tr>
<td>Number of leads</td>
<td>≥ 7</td>
<td>≥ 7</td>
<td>≥ 4</td>
<td>1-2(*)</td>
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<tr>
<td>Types of leads</td>
<td>EEG, EOG, EMG, ECG, Airflow, Effort, Oximetry</td>
<td>EEG, EOG, EMG, ECG, Airflow, Effort, Oximetry</td>
<td>ECG, Airflow, Oximetry and other respiratory movements</td>
<td>Oximetry and other respiratory movements</td>
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<td>Study position</td>
<td>Objective</td>
<td>Maybe</td>
<td>Maybe</td>
<td>Not measured</td>
</tr>
<tr>
<td>Setting</td>
<td>Unattended</td>
<td>Attended or Unattended</td>
<td>Attended or Unattended</td>
<td>Attended or Unattended</td>
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<tr>
<td>Description</td>
<td>Standard Sleep Study performed at a sleep laboratory, studies done while sleeping</td>
<td>Comprehensive portable PSG</td>
<td>Portable testing related to sleep disorders</td>
<td>Continuous recording of 1-2 signals (i.e., airway occlusion, oxygen saturation, electrocardiogram)</td>
</tr>
</tbody>
</table>


european respiratory society every breath counts
Figure 5

DIAGNOSIS ALGORITHM

Figure 6

TREATMENT CHOICE ALGORITHM
**Figure 7**

**HYPOVENTILATION MECHANISMS**

- **OHS**
  - ↑ Mechanical load
  - ↑ Work breathing
  - Muscle deficiency
  - Leptin resistance
  - Breathing sleep disorders
  - REM hypoventilation
  - Sleep hypercapnia
  - Chemoreceptor blunting
  - Daytime hypercapnia
  - NIV action
  - CPAP action

- **NIV**
- **CPAP**

**Figure 8**

**OHS MANAGEMENT ALGORITHM**

- **OHS**
  - AHI < 30
  - AHI ≥ 30
  - NIV
  - CPAP
  - CPAP Responders
  - CPAP non Responders
  - Following CPAP
  - NIV

*JF Masa. Restrictive Lung Disorders. In: M Kryger. Principles and practice in sleep medicine 2011*

*European Respiratory Society. Every Breath Counts*
SLEEP APNEA AND THE OBESITY-HYPOVENTILATION SYNDROME

J. F. Masa
“San Pedro de Alcántara” Hospital
Cáceres. Spain

OSA DEFINITION

- Disorder characterized by excessive sleepiness, cognitive-behavioral, respiratory, cardiac, metabolic or inflammatory alterations secondary to repeated episodes of upper airway obstruction during sleep.

- These episodes are measured with the AHI. An AHI > 5 associated with symptoms related to the disease and unexplained by other causes confirms the diagnosis.


Epidemiology

Global prevalence = 21%

Global prevalence = 27%

Table 4: Age-Specific Estimates of Sleep-Disordered Breathing in the General Population, According to Gender, Hypoventilation Index and Disease

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Hypoventilation Index</th>
<th>Prevalence (%)</th>
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<tbody>
<tr>
<td>20-24</td>
<td>40-49</td>
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<td>25-29</td>
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</tr>
<tr>
<td>30-34</td>
<td>60-69</td>
<td>7.4</td>
</tr>
<tr>
<td>35-39</td>
<td>70-79</td>
<td>8.5</td>
</tr>
<tr>
<td>40-44</td>
<td>80-89</td>
<td>9.6</td>
</tr>
<tr>
<td>45-49</td>
<td>90-99</td>
<td>10.7</td>
</tr>
<tr>
<td>50-54</td>
<td>100-109</td>
<td>11.8</td>
</tr>
<tr>
<td>55-59</td>
<td>110-119</td>
<td>12.9</td>
</tr>
<tr>
<td>60-64</td>
<td>120-129</td>
<td>14.0</td>
</tr>
<tr>
<td>65-69</td>
<td>130-139</td>
<td>15.1</td>
</tr>
<tr>
<td>70-74</td>
<td>140-149</td>
<td>16.2</td>
</tr>
<tr>
<td>75-79</td>
<td>150-159</td>
<td>17.3</td>
</tr>
<tr>
<td>80-84</td>
<td>160-169</td>
<td>18.4</td>
</tr>
<tr>
<td>85-89</td>
<td>170-179</td>
<td>19.5</td>
</tr>
<tr>
<td>90+</td>
<td>180-189</td>
<td>20.6</td>
</tr>
</tbody>
</table>


Table 5: Global Prevalence of Sleep-Disordered Breathing in the General Population

<table>
<thead>
<tr>
<th>Region</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North</td>
<td>20</td>
</tr>
<tr>
<td>South</td>
<td>21</td>
</tr>
<tr>
<td>East</td>
<td>22</td>
</tr>
<tr>
<td>West</td>
<td>23</td>
</tr>
</tbody>
</table>

Global prevalence = 21%

Global prevalence = 27%

Prevalence of disease: 95% confidence interval

Global prevalence = 21%

Global prevalence = 27%

Prevalence of disease: 95% confidence interval
**Risk Factors**

- AGE AND SEX
- OBEISITY
- GENETIC FACTORS
- FACIAL DEFORMITIES
- OTHER DISEASES

**Aggravating Factors**

- ALCOHOL, TOBACCO
- RESPIRATORY DEPRESSORS
- SLEEP POSITIONS (DECUBITUS-SUPINE)

---

**STARLING RESISTOR MODEL OF OSA**

- Rigid tube
- Sealed box
- Collapsible segment
- Upstream $P_{in}$
- Downstream $P_{out}$

---

**NTOSSEIS OF CYCLICAL OSA**

- Sleep and Oxygenation
- Hypoxia
- Respiratory Distress
- Stroke
- Cardiac Failure
- Hypertension
- Daytime Sleepiness

---

*Dempsey JA et al. Physiol Rev 2010;90:47-112*
PATHOGENESIS

A: midsagittal magnetic resonance image (MRI) in a normal subject (left) and in a patient with severe OSA (right).

CLINICAL FEATURES OF OSA

MORPHOTYPE
MALE
MIDDLE-AGED
OBSE
WIDE NECK

SYMPTOMS
IRREGULAR SNORING
ASPHYXIA EPISODES
EXCESSIVE DAYTIME SLEEPINESS
RESTLESS SLEEP

Sleep apnea symptoms

NIGHT
• Snore
• Observed Apneas
• Asphyxia Episodes
• Abnormal Movements
• Diaphoresis
• Frequent Awakenings
• Nocturia or Enuresis
• Nightmares
• Restless Sleep
• Insomnia
• Gastroesophageal Reflux

DAYTIME
• Excessive Daytime Sleepiness
• Feeling Restless Sleep
• Chronic Fatigue
• Morning Headache
• Irritability
• Apathy
• Depression
• Difficulty Concentrating
• Memory Loss
• Decreased Libido
EPWORTH SLEEPINESS SCALE

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would affect you. Use the following scale to circle the most appropriate number for each situation:

0 = would never doze or fall asleep
1 = slight chance of dozing or falling asleep
2 = moderate chance of dozing or falling asleep
3 = high chance of dozing or falling asleep

<table>
<thead>
<tr>
<th>Situation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Sitting and reading</td>
<td>0</td>
</tr>
<tr>
<td>2. Watching TV</td>
<td>0</td>
</tr>
<tr>
<td>3. Sitting, inactive in a public place [e.g., a theater, a meeting, or a park]</td>
<td>0</td>
</tr>
<tr>
<td>4. As a passenger in a car for an hour without a break</td>
<td>0</td>
</tr>
<tr>
<td>5. Lying down to rest in the afternoon when circumstances permit</td>
<td>0</td>
</tr>
<tr>
<td>6. Sitting and talking to someone</td>
<td>0</td>
</tr>
<tr>
<td>7. Sitting quietly after a lunch without alcohol</td>
<td>0</td>
</tr>
<tr>
<td>8. In a car, while stopped for a few minutes in traffic</td>
<td>0</td>
</tr>
</tbody>
</table>

PATIENTS WITH HIGH RISK OF SLEEP APNEA IN WHOM RELATED SYMPTOMS SHOULD BE EVALUATED

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity (BMI &gt; 35)</td>
</tr>
<tr>
<td>Cardiac insufficiency</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Refractory hypertension</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
</tr>
<tr>
<td>Nocturnal arrhythmias</td>
</tr>
<tr>
<td>Cerebrovascular accidents (stroke, TIA)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>Individual with high risk of accidents</td>
</tr>
<tr>
<td>Pre-operative bariatric surgery</td>
</tr>
<tr>
<td>Chronic respiratory diseases with greater gasometric deterioration than expected</td>
</tr>
</tbody>
</table>

CARDIOVASCULAR CONSEQUENCES

Hypertension
OSEA AND CARDIOVASCULAR DISEASE

FEATURES
- Hypoxemia
- Hypercapnia
- Reoxygenation
- Intrapulmonary pressure changes
- Microarousals

INTERMEDIATE MECHANISMS
- Sympathetic activation
- Endothelial dysfunction
- Oxidative stress
- Inflammation
- Hypercoagulability
- Metabolic dysregulation

CARDIOVASCULAR CONSEQUENCES
- Systemic hypertension
- Arteriosclerosis
- Arrhythmia
- Myocardial ischemia
- Stroke
- Heart failure

EFFECT MAGNITUDE

- 2 mm Hg reduction in diastolic blood pressure on a population basis would result in:
  - 17% decrease in the prevalence of hypertension
  - 16% reduction in the risk of coronary heart disease
  - 15% reduction in the risk of stroke and transient ischemic attack

**CPAP COMPLIANCE**

More benefit in patients with higher baseline BP, higher BMI, and more severe OSA


**SLEEPINESS**

Masa JF et al, SLEEP 2006, 29(11):1463-1468

**WITHOUT SLEEPINESS**

359 paucisymptomatic patients

<table>
<thead>
<tr>
<th>TABLE 5. FOLLOW-UP CHANGE IN BLOOD PRESSURE, BY TREATMENT COMPLIANCE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source Blood Pressure</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Hours</td>
</tr>
<tr>
<td>16.00</td>
</tr>
<tr>
<td>12.00</td>
</tr>
</tbody>
</table>

*Selection of variables: CI = confidence interval; Coeff = coefficient.

CPAP IN OSA WITH RESISTANT HYPERTENSION: RCT

N: 210 patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Control Group</th>
<th>CPAP Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAS</td>
<td>0.006</td>
<td>0.001</td>
</tr>
<tr>
<td>TAD</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

CONTROL GROUP

CPAP GROUP

NOVO HYPERTENSION

340 patients with "novo" hypertension and OSA. 12 weeks of follow-up

Mean AHI: 29, Eight weeks RCT crossover trial
OSA AND HYPERTENSION: CONCLUSIONS

• RCT showed that CPAP reduces blood pressure in OSAS patients
• CPAP could play a role in the management of hypertension, also in patients with resistant hypertension
• The effect of CPAP on blood pressure is directly related to treatment compliance

CARDIOVASCULAR CONSEQUENCES

LONG-TERM MORTALITY IN MEN, WOMEN AND ELDERLY

Mortality

MEN
1651

WOMEN
1116

ELDERLY
936

Marín JM et al. Lancet 2005
Martínez-García MA et al. AJRCCM 2012
CARDIOVASCULAR MORTALITY: CONCLUSIONS

- Observational studies suggest that CPAP reduces mortality and cardiovascular events
- There is currently not enough evidence to support CPAP treatment for primary or secondary CVE prevention
- Large multicenter RCT’s are ongoing

TRAFFIC ACCIDENTS

TRAFFIC ACCIDENT RISK IN SLEEP APNEA

<table>
<thead>
<tr>
<th>Location</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friday 100</td>
<td>7.43 (1.46–37.36)</td>
</tr>
<tr>
<td>Madrid 100</td>
<td>2.22 (0.28–17.58)</td>
</tr>
<tr>
<td>Vila-seca 100</td>
<td>8.21 (3.46–19.96)</td>
</tr>
<tr>
<td>Lleida 5000</td>
<td>8.77 (1.01–78.06)</td>
</tr>
<tr>
<td>Bergamo 000</td>
<td>3.94 (1.20–13.07)</td>
</tr>
<tr>
<td>Combined total</td>
<td>2.36 (1.56–3.58)</td>
</tr>
</tbody>
</table>

DIAGNOSIS

PSG VS PM

- SAS prevalence: 25% (with and without symptoms)
- PSG:
  - Expensive
  - Complex and time consuming
  - It cannot cover all needing population.
- Advantages of simplified devices (HRP and HNP):
  - Less expensive
  - Less complex and more rapid performing
  - It can cover a wider needing population.

SLEEP STUDY METHODS

<table>
<thead>
<tr>
<th>Types of leads</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
<th>Type 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEG, EOG, EMG, ECG, Airflow, Effort, Oximetry</td>
<td>EEG, EOG, EMG, ECG, Airflow, Effort, Oximetry</td>
<td>ECG, Airflow, Effort, Oximetry</td>
<td>Oximetry and other respiratory airflow</td>
<td>Oximetry and other respiratory airflow</td>
</tr>
<tr>
<td>Body position</td>
<td>Obliquely measured</td>
<td>Maybe</td>
<td>Maybe</td>
<td>Not measured</td>
</tr>
<tr>
<td>Setting</td>
<td>Attended (usually in a sleep center)</td>
<td>Unattended</td>
<td>Attended or Unattended</td>
<td>Attended or Unattended</td>
</tr>
<tr>
<td>Description</td>
<td>Standard PSG performed in a sleep laboratory, refers to standard portable PSG</td>
<td>Comprehensive portable PSG</td>
<td>Portable testing by the sleep center</td>
<td>Comprehensive recording of 1-2 signals, usually performed in the home or office setting</td>
</tr>
</tbody>
</table>
COSTS FROM HRP RELATED TO PSG

Percentages of total HRP cost and their distribution in three groups (test cost, patients' cost and cost for equal efficacy) compared with polysomnography costs, which is considered to be 100%.


THERAPEUTIC DECISION AGREEMENT

Masa JF et al. Am J Respir Crit Care Med. 2011;184(8):964-71

DIAGNOSIS ALGORITHM

Masa JF et al. Am J Respir Crit Care Med. 2011;184(8):964-71
**TREATMENT CHOICE**


**MANDIBULAR ADVANCEMENT DEVICES**

SURGICAL TREATMENT OF SLEEP APNEA

Types
- Bypass surgery: Tracheotomy
- Content reduction surgery
  - Adenoid-tonsillectomy (for children)
  - Nasal Surgery
  - Resection Surgery (base of the tongue)
  - Palate surgery
- Dilator surgery
  - Maxillo-mandibular

Indications
ADULTS
- Treatment for improving CPAP tolerance
- Must be performed in selected cases

CHILDREN
- It's the treatment and healing choice in 75% cases

OBESITY HYPOVENTILATION SYNDROME
OHS

OHS DEFINITION
- Daytime hypercapnic respiratory failure (PCO2 > 45), obesity (BMI > 30) and sleep disorders.
- It is necessary to exclude lung, neuromuscular, metabolic and chest diseases before making an OHS diagnosis.

**PREVALENCE**

- It is unknown in general population
- In patients with suspected sleep apnea: 10-30%
- In subjects with unknown sleep apnea: 9%-14%
- In subjects referred to bariatric surgery: 7%-22%

---

**HYPOVENTILATION MECHANISMS**

- OHS
- Breathing sleep disorders
- Sleep apnoea
- Sleep hypercapnia
- Daytime hypercapnia
- Chemoreceptor blunting
- Increased bicarbonate

---

**NOCTURNAL CO2 ACUMULATION**

LUNG VOLUMES, RESPIRATORY MECHANICS, AND VENTILATORY RESPONSE IN OBESE PATIENTS WITH AND WITHOUT HYPOVENTILATION SYNDROME

<table>
<thead>
<tr>
<th></th>
<th>BMI Kg/m²</th>
<th>FRC %pr</th>
<th>TLC %pr</th>
<th>Crs cmH₂O L⁻¹</th>
<th>Res cmH₂O L⁻¹</th>
<th>WOB J/L</th>
<th>ΔV'/ΔPCO₂ l/min mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>24</td>
<td></td>
<td></td>
<td>1.2</td>
<td>0.43</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>OB</td>
<td>45</td>
<td>85</td>
<td>95</td>
<td>5.0</td>
<td>0.74</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>OH</td>
<td>46</td>
<td>83</td>
<td>83</td>
<td>7.8</td>
<td>1.64</td>
<td>0.9</td>
<td></td>
</tr>
</tbody>
</table>

Rochester DF et al. 1985

TREATMENT

• Diet:
  - Respiratory insufficiency, pulmonary hypertension and sleep disorders can be reversed if patients achieve a normal weight.
  - However, only a few maintain a significant weight reduction for a long period.

• Bariatric surgery:
  - Less data are available, especially as regards the long-term consequences.
  - Moreover, bariatric surgery can be an alternative for only a minority of OHS patients due to the morbidity and mortality inherent in the surgical procedure itself.
NIV: HOSPITAL ADMISSIONS

OHS patients treated with CPAP or NIPPV:
70% reduction in hospital stays after treatment

Berg G et al. Chest 2001; 120:377

NIV: SURVIVAL

Composition from observed survival in studies with treated and untreated patients with NIV


CPAP VS NIV

Selected patients

OHS MANAGEMENT ALGORITHM

OHS

CPAP

NIV

Follow with CPAP

o NIV Responders
o CPAP Responders

ERS

excess respiratory sound every breath counts
Perioperative problems in obese patients

Prof. Paolo Pelosi
University of Genoa
IRCCS & IST
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Largo Rosanna Benzi 8
16132 Genoa
Italy
ppelosi@hotmail.com
The Morbidly Obese Patient and PPCs

Department of Surgical Sciences and Integrated Diagnostics (DISC)
University of Genoa, Italy

ppelosi@hotmail.com

ERS Barcelona 2013

Agenda

- Morbidity and mortality: Periop and ICU
- Anesthesia and the respiratory function
- nCPAP/NPPV at intubation
- Recruitment and PEEP
- Protective ventilation
- Prone position
- Post-Operative period: Positioning and Physio

Outcomes of Morbidly Obese Patients Receiving Invasive Mechanical Ventilation: A Nationwide Analysis


% of morbidly obese persons who were hospitalized

% of morbidly obese persons who were ventilated

Year
Outcomes of Morbidly Obese Patients Receiving Invasive Mechanical Ventilation: A Nationwide Analysis


Pulmonary Complications: The Role of Obesity Prolonged MV after Surgery

Helling TS et al. Obes Surg 2006;14:1036-41

Table 3. Univariate analysis of perioperative factors possibly involved in need for prolonged mechanical ventilation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Odds ratio</th>
<th>95% Confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>2.23</td>
<td>0.48 – 0.749</td>
<td>0.62</td>
</tr>
<tr>
<td>Age &lt;50 years</td>
<td>1.05</td>
<td>0.97 – 0.986</td>
<td>0.15</td>
</tr>
<tr>
<td>BMI &gt;30</td>
<td>2.92</td>
<td>0.96 – 0.754</td>
<td>0.01</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>2.30</td>
<td>0.83 – 0.769</td>
<td>0.02</td>
</tr>
<tr>
<td>Revision surgery</td>
<td>1.88</td>
<td>0.97 – 0.897</td>
<td>0.11</td>
</tr>
<tr>
<td>Reoperation</td>
<td>2.00</td>
<td>1.06 – 2.157</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Morbid obesity is an independent risk factor of death among surgical critically ill patients

Nasraway et al. Crit Care Med 2006;34:964-970
Effect of obesity on intensive care morbidity and mortality: A meta-analysis

Obesity in critically ill patients is associated with:
- Excess mortality
- Prolonged duration of mechanical ventilation
- Prolonged intensive care unit length of stay

Influence of body mass index on outcome of the mechanically ventilated patients
Anzueto et al Thorax published online October 27, 2010

Adjusted OR for the development of ARDS

There were no differences in outcomes (duration of mechanical ventilation, length of stay and mortality in intensive care unit and hospital)

Agenda
- Morbidity and mortality: Periop and ICU
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- nCPAP/NPPV at intubation
- Recruitment and PEEP
- Protective ventilation
- Prone position
- Post-Operative period: Positioning and Physio
**Lung volume as a function of obesity**


![Graph showing lung volume as a function of BMI](image1)

- $r = 0.86$
- $p < 0.01$

**Obesity and post-operative atelectasis**


- **Obese**
- **Non-obese**

- Before induction
- After extubation
- 24 hours later

**Obesity Increases Post-op Work of Breathing**


![Graph showing work of breathing](image2)

- $r = 0.86$
- $p < 0.01$
Obesity and post-operative PFTs

Agenda
- Morbidity and mortality: Periop and ICU
- Anesthesia and the respiratory function
- nCPAP/NPPV at intubation
- Recruitment and PEEP
- Protective ventilation
- Prone position
- Post-Operative period: Positioning and Physio

Prevention of atelectasis during the induction of anesthesia in obese
Noninvasive Ventilation and Alveolar RM Improve Respiratory Function During and After Intubation of Morbidly Obese Patients: a RCT
Futier E, Pelosi P, Jaber S et al. Anesthesiology 2011 114: 1354-1363

Agenda
- Morbidity and mortality: Periop and ICU
- Anesthesia and the respiratory function
- nCPAP/NPPV at intubation
- Recruitment and PEEP
- Protective ventilation
- Prone position
- Post-Operative period: Positioning and Physio
**EFFECTS OF PEEP DURING GENERAL ANESTHESIA**

Paolo Pelosi, Claudia Brusasco and Henrik Reinus
Chapter, Springer Verlag 2012

[Diagram showing effects of PEEP on lung recruitment in normal weight and morbidly obese patients]

**Description of anesthesia practice of ventilatory management during general anesthesia in operating room**

Jaber S et al. Anaesthesia. 2012 Sep;67(9):999-1008

Prospective multicenter observational French study (Jaber S et al): 2961 patients from 49 anesthesia departments

![Bar chart showing recruitment (RM) and PEEP distribution]

PEEP and RM are rarely used, whatever the type of surgery

**Tidal volume in obese in operating room?**

Jaber S et al. Anaesthesia. 2012 Sep;67(9):999-1008

423/2961 obese patients: 16%

![Graphs showing tidal volume (VT) measured and calculated Ideal Body Weight (IBW) in obese patients]
Recruitment Maneuvres in Morbidly Obese Patients During General Anaesthesia

Prevention of Atelectasis in Morbidly Obese Patients during General Anesthesia and Paralysis

Agenda

- Morbidity and mortality: Periop and ICU
- Anesthesia and the respiratory function
- nCPAP/NPPV at intubation
- Recruitment and PEEP
- Protective ventilation
- Prone position
- Post-Operative period: Positioning and Physio

Lower Tidal Volumes in Patients without Preexisting Lung Injury
Ventilation strategies in obese pts. undergoing surgery: a quantitative systematic review and meta-analysis

**Intraoperative PaO₂**

<table>
<thead>
<tr>
<th>Study or Cohort</th>
<th>Mean SD</th>
<th>Total</th>
<th>Mean SD</th>
<th>Total</th>
<th>Mean Difference</th>
<th>N</th>
<th>Standard Error</th>
<th>95% Confidential Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcomes 2007</td>
<td>10.1 0.7</td>
<td>50</td>
<td>10.6 0.7</td>
<td>50</td>
<td>0.53 (0.28)</td>
<td>40</td>
<td>0.31</td>
<td>0.02, 1.05</td>
</tr>
<tr>
<td>Talab 2008</td>
<td>10.5 0.6</td>
<td>26</td>
<td>11.3 0.7</td>
<td>25</td>
<td>0.8 (0.42)</td>
<td>50</td>
<td>0.32</td>
<td>0.15, 1.47</td>
</tr>
<tr>
<td>Total</td>
<td>10.4 0.7</td>
<td>76</td>
<td>10.6 0.7</td>
<td>75</td>
<td>0.27 (0.44)</td>
<td>90</td>
<td>0.34</td>
<td>0.03, 0.49</td>
</tr>
</tbody>
</table>

**Intraoperative Compliance**

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean SD</th>
<th>Total</th>
<th>Mean SD</th>
<th>Total</th>
<th>Mean Difference</th>
<th>N</th>
<th>Standard Error</th>
<th>95% Confidential Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talab 2007</td>
<td>5.7 0.6</td>
<td>92</td>
<td>6.2 0.7</td>
<td>90</td>
<td>0.52 (0.32)</td>
<td>182</td>
<td>0.20</td>
<td>0.19, 0.84</td>
</tr>
<tr>
<td>Talab 2008</td>
<td>5.2 0.7</td>
<td>12</td>
<td>5.1 0.7</td>
<td>13</td>
<td>0.1 (0.42)</td>
<td>25</td>
<td>0.32</td>
<td>0.13, 0.19</td>
</tr>
<tr>
<td>Total</td>
<td>5.4 0.7</td>
<td>104</td>
<td>5.6 0.7</td>
<td>103</td>
<td>0.2 (0.44)</td>
<td>187</td>
<td>0.23</td>
<td>0.09, 0.35</td>
</tr>
</tbody>
</table>

**Recruitment Maneuver and PEEP are not effective during laparoscopic bariatric surgery**
Whalen et al Anesth Analg 2006;102:298-305

- Vasopressors treatments were larger in RM/PEEP group
- The effects of RM/PEEP were promptly dissipated in the immediate postoperative period

**Intraoperative Ventilatory Strategies for Prevention of Pulmonary Atelectasis in Obese Patients Undergoing Laparoscopic Bariatric Surgery**

Alveolar-to-arterial oxygen gradient (mm Hg), 22 pts per group
Rationale and study design of PROVHILO - a worldwide multicenter randomized controlled trial on protective ventilation during general anesthesia for open abdominal surgery.


Which ventilation setting during general anesthesia?

Shultz MJ et al Anesthesiology 2007; 106;1226.1231
Pelosi P and Rocco PR. Anesthesiology 2011: 115: 923-925

- Tidal Volume < 10 ml/Kg PBW
- Increase RR to control pHa/PaCO2
- Plateau Pressure < 25-30 cmH2O
- PEEP > 5 cmH2O
- RM 35-40 cmH2O – PEEP/VT – PC/VC
- Monitor Paw-Time/Check PEEPi

Agenda

- Morbidity and mortality: Periop and ICU
- Anesthesia and the respiratory function
- nCPAP/NPPV at intubation
- Recruitment and PEEP
- Protective ventilation
- Prone position
- Post-Operative period: Positioning and Physio
Prone position does not affect respiratory function in obese


Feasibility and effectiveness of prone position in morbidly obese ARDS patients: a case-control clinical study.

Feasibility and effectiveness of prone position in morbidly obese ARDS patients: a case-control clinical study.

\( \chi^2 = 4.9601, p = 0.0259 \).
**Agenda**

- Morbidity and mortality: Periop and ICU
- Anesthesia and the respiratory function
- nCPAP/NPPV at intubation
- Recruitment and PEEP
- Protective ventilation
- Prone position
- Post-Operative period: Positioning and Physio

---

**Eliminating respiratory intensive care unit stay after gastric bypass surgery**

Hallowell PT et al Surgery 2007;142:608-12

Mandatory OSA screening and aggressive preoperative treatment have eliminated the need for respiratory-related ICU stays after bariatric surgery.

![Bar chart showing patients recovered in ICU (%)](image)

---

**Respiratory Physiotherapy**


- Early Mobilization
- Deep-Breathing
- Cough

**Incentive Spirometry**
Efficacy of chest physiotherapy (coughing, deep breathing, early mobilization) after major abdominal surgery in obese


Postoperative Pulmonary Complications following Abdominal Surgery

<table>
<thead>
<tr>
<th></th>
<th>OBESE</th>
<th>NORMAL</th>
<th>OBESE in PICU</th>
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<td>50%</td>
<td>20%</td>
<td>7%</td>
</tr>
<tr>
<td>PNEUMONIA</td>
<td>40%</td>
<td>15%</td>
<td>10%</td>
</tr>
</tbody>
</table>


Treatment options for the obese patient

A/Professor Lisa Wood
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Hunter Medical Research Institute
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Aims
1. To consider the evidence surrounding the use of weight loss interventions in COPD and asthma.
2. To consider suitable approaches to weight loss in COPD and asthma.
3. To review the role of diet quality in COPD and asthma.

Summary

Obesity and chronic disease
'The global epidemic of overweight and obesity - "globesity" - is rapidly becoming a major public health problem in many parts of the world. Paradoxically coexisting with undernutrition in developing countries, the increasing prevalence of overweight and obesity is associated with many diet-related chronic diseases including diabetes mellitus, cardiovascular disease, stroke, hypertension and certain cancers.'[1]. The mechanism by which obesity increases the risk of co-morbid diseases is not completely understood, but it is believed that inflammation plays an important role [2]. Adipose tissue produces and secretes a number of adipokines and inflammatory mediators and is considered to be an endocrine organ. Hence, obesity is characterised by a low-grade systemic inflammation, indicated by elevated serum levels of inflammatory markers such as IL-6, CRP and TNF-α [3, 4], which increases risk of disease.

COPD

A. Effects of obesity
Obesity prevalence estimates in COPD vary, ranging from 18% (Netherlands)[5] to 54% (USA)[6]. Obesity complicates COPD management and is associated with decreased expiratory reserve volume (ERV) and functional residual capacity (FRC), increased use of inhaled medications, increased dyspnoea and fatigue and decreased health related quality of life. In terms of exercise performance, obesity is associated with decreased weight bearing exercise capacity, although peak cycle exercise capacity is unchanged [7-9].

The ‘obesity paradox’ exists in COPD. This refers to the observation that while in the general population obesity increases mortality risk, obesity is associated with increased survival in COPD [10]. However, this relationship differs significantly with stage of COPD. In mild and moderate COPD there is a non-significant U-shaped relationship, with the lowest risk occurring in normal-weight to overweight subjects, whereas in severe COPD, mortality continues to decrease with increasing BMI. Similar results have been reported for COPD-related deaths, with the strongest association with BMI found in severe COPD[11].

The mechanisms by which obesity is protective in COPD are unclear. Indeed, obesity increases systemic inflammation in COPD, with increased TNF-α, IL-6 and leptin, which increases risk of comorbidities [12]. However, obesity also reduces static lung volumes, which has been associated with improved COPD survival [13]. In addition, obesity increases fat free mass (FFM)[12] due to over-nutrition (increased protein and micronutrient intake) as well as increased weight bearing. This provides benefits such as maintenance of muscle function. Hence, it is likely that different features of obesity may be more important at different disease stages. In early stages of disease, the negative long term effects of obesity may be most important, as increased fat mass and systemic inflammation increase the risk of insulin resistance, CVD and diabetes. In more severe disease, the positive effect of increased fat free mass that accompanies obesity is likely to be most important, due to maintenance of muscle function, which reduces risk of death.
B. Management of obesity

Weight loss in COPD:
Considering the known protective effect of FFM in COPD, weight loss should be approached with caution. Weight loss, via calorie restriction alone, will lead to FFM loss, hence a multi-component weight loss approach is warranted. A weight loss strategy is currently under evaluation (HMRI, Newcastle, Australia) that includes three components:
1. **Calorie restriction**: reduce intake of nutrient-poor foods (those high in saturated fat and refined carbohydrates, eg take away foods). Replace with nutrient-rich foods (lean protein, fruit and vegetables).
2. **High protein**: (1.2-1.5g protein per kg ideal body weight): protein intake may be boosted using easily accessible foods, e.g. skim milk powder, custard, milkshakes, eggs, or oral supplement.
3. **Resistance training**: is important as dietary restriction alone leads to loss of muscle mass, as well as fat mass, so MUST be done in combination with increased physical activity and adequate protein intake, to ensure muscle mass is maintained.

Increased protein intake, combined with increased physical activity, will encourage the development of muscle mass, whilst calorie restriction will facilitate loss of fat mass.

Effect of obesity on COPD pulmonary rehabilitation outcomes
Obesity and overweight do not diminish responses to pulmonary rehabilitation [14]. Hence rehabilitation programmes may provide a suitable vehicle for implementing weight loss interventions, although to date there is no proven efficacy for achieving weight loss with this approach.

Smoking cessation and obesity:
Smoking cessation and weight management/ loss can be difficult to undertake at the same time, as both require a lot of effort and commitment. Smoking cessation is often linked with weight gain and is often a serious concern for smokers. There are several reasons why people gain weight when they quit smoking, including:
- Nicotine withdrawal: Nicotine increases the metabolic rate, so smoking cessation can slow the metabolism.
- Increased appetite: Smoking cessation can increase appetite, which eventually returns to normal.
- Replacing smoking with food: Increased food intake may occur if food replaces the smoking habit.

*Advise patients*: Continued smoking has worse effects than a small weight gain. You would need to gain > 40kgs above recommended weight to equal the same risk of heart disease posed by smoking.

Summary of obesity management in COPD
- The effects of weight loss in obese COPD are unknown. No recommendations currently available.
- Considering the improved prognosis for COPD patients with increasing BMI, weight loss strategies need to be considered with caution.
- A weight loss study, combining calorie reduction, high protein intake and resistance training, is currently underway.
- COPD pulmonary rehabilitation programmes, involving exercise training and nutritional counselling, provide an opportunity for administering weight loss interventions, but to date have no proven efficacy in achieving weight loss.
- Other strategies for achieving weight loss: eg pharmacotherapy or bariatric surgery have not been tested in COPD.
Asthma

A. Effects of obesity
Obesity/overweight increases asthma risk by 40-90%. The mechanisms driving this association are unknown, but likely to include both anatomical and inflammatory effects. Obesity complicates asthma management, with changes in respiratory physiology, including reduced dynamic lung function (forced expiratory volume in 1 second, FEV1 and forced vital capacity, FVC) [15-17], reduced static lung volumes (ERV and FRC) [18,19] and reduced respiratory muscle strength [20, 21]. Obese patients also have reduced exercise capacity [22] and an increase in dyspnoea and wheezing [23]. In addition, obese asthma is characterised by drug resistance. In comparison to non-obese patients, obese asthmatics report more continuous symptoms, miss more work, and use more inhalers [24].

B. Management of obesity

Weight loss in asthma:

Option 1: Bariatric Surgery: Overall, the literature demonstrates clear improvements in asthma outcomes following bariatric surgery [25-27]. The follow-up periods for these studies range from 1 to 7.3 years, with weight loss of 5.4-20.3 kg/m2 and various outcomes improved, including asthma symptoms, medication use and lung function. However, bariatric surgery is not indicated for the majority of overweight and obese asthmatics, being recommended for subjects with BMI >35 (if one or more comorbidities are present) or 40 kg/m2 (with or without comorbidities).

Option 2: Lifestyle Intervention: Calorie restriction: Most dietary restriction studies in asthma have used a non-randomised design, with intervention periods range from 6-14wks, weight loss of 8-14.5% and improvements in lung function, symptoms and quality of life. Only one randomised controlled weight loss trial has been conducted in adults with asthma, resulting in significant improvements in lung function and significantly fewer asthma exacerbations in the year following the intervention [28]. Another recent randomised weight loss intervention in overweight and obese asthmatic adults, compared 3 types of weight loss interventions: dietary restriction, exercise and combined diet and exercise [29]. This study achieved weight loss of -8.4%, -1.8% and -8.2% in the dietary, exercise and combined interventions respectively. This corresponded with improvements in asthma control after the dietary and combined interventions, while quality of life improved after the dietary, exercise and combined interventions. A 5-10% weight loss resulted in clinically important improvements to asthma control in 58% of subjects and quality of life in 83% of subjects. This study suggests a weight loss goal of 5-10% should be recommended to assist in the clinical management of overweight and obese adults with asthma [29].

Summary of obesity management in asthma:

- Obesity complicates asthma management.
- Bariatric surgery improves asthma in the morbidly obese.
- Diet and exercise intervention is effective in improving asthma outcomes in overweight and mildly obese subjects.
- Even a small amount of weight loss can improve asthma outcomes: 5-10% weight loss should be advocated, as this is a realistic goal (with dietetic input) and results in clinically improved quality of life and asthma control in the majority of patients.
- The effects of pharmacological weight loss interventions in asthma are unknown.

Diet Quality

The obesogenic diet is characterized by macronutrient surplus, as obesity is driven by excessive consumption of energy-yielding nutrients. In addition, the obesogenic diet is typically poor in quality, with increased consumption of processed or ‘fast’ foods, reduced fruit, vegetable and wholegrain intake. As a result, nutrient profiles are disturbed, with high dietary intake of saturated fat and low intake of antioxidants and fibre.
A. Antioxidants
Antioxidants can be obtained from the diet, being primarily found in fruit, vegetables, nuts and wholegrains. They are relevant to COPD and asthma, as they protect cells from the damaging effects of free radicals, which are produced in excess in both COPD and asthma due to the chronic activation of inflammatory cells. Oxidative stress is increased in both COPD [30] and asthma [31] and antioxidant defences, including carotenoids (which are primarily found in fruit and vegetables), are reduced in asthma [32] compared to controls. This is despite similar dietary intake, suggesting increased utilization of carotenoids in the presence of an increased oxidative burden[32]. Antioxidant manipulation has been shown to modify asthma outcomes. Asthmatic subjects consumed a low antioxidant diet for 10 days and this resulted in a worsening of neutrophilic airway inflammation, lung function and asthma symptoms [33]. Furthermore, in a recent RCT, after 14 days, subjects consuming a low fruit and vegetable (F&V) diet had reduced %FEV1 and %FVC compared to subjects on a high F&V diet. At the end of the trial, there was an increase in time to exacerbation in the high F&V diet group compared to the low F&V diet group, with the low F&V diet group being 2.26 times more likely to exacerbate [34].

B. Fibre
Soluble fibre has been shown to have anti-inflammatory effects following fermentation by bacteria in the gut to produce short chain fatty acids (SCFA). These SCFA activate GPR43 resulting in the production of anti-inflammatory mediators. Thus, low fibre diets lead to loss of GPR43 activity and a reduction in anti-inflammatory mediators. This has been shown to affect the airways, in some experiments conducted in GPR43 -/- vs wild type mice, where bronchoalveolar lavage cell counts and eosinophil peroxidase activity were increased in the absence of GPR43 [35]. A protective role of fibre has been observed in COPD, where lower fibre intakes were associated with risk of COPD [36]. Similarly, subjects with severe persistent asthma were shown to consume less fibre than healthy controls and lower fibre intakes were associated with lower FEV1 and airway eosinophilia [37].

C. Dietary fat
Fatty acids are an essential dietary component, providing the key energy source in vivo. They are also essential for body functions such as formation and functioning of cell membranes and the nervous system. Fatty acids are comprised of a hydrocarbon chain, of varying length and degree of saturation. Saturated fatty acids (SFA) have no double bonds in the carbon chain. Monounsaturated fatty acids (MUFA) have one double bond. Polyunsaturated fatty acids (PUFA) have more than one double bond. PUFA can be further classified as n-3 PUFA or n-6 PUFA, depending on the position of the first double bond. In general, SFA and n-6 PUFA have been shown to have inflammatory effects, while MUFA and n-3 PUFA have various anti-inflammatory actions. Consumption of excess dietary fat can interfere with normal physiological processes. Fatty acids can modulate inflammatory responses via a variety of mechanisms. They can directly induce Toll-like receptors (TLRs) and lipid sensors, they can transmit stress signals following binding to fatty acid binding proteins (FABPs) and they can activate/inhibit nuclear receptors that modulate inflammation. They can also induce endoplasmic (ER) stress, activating the unfolded protein response. This leads to activation of the transcription factors which can modify intracellular lipid metabolism [38].

Dietary fat has been shown to induce airway inflammation in asthmatics [39]. Stable asthmatics were challenged with a high versus low fat meal and airway inflammation was monitored for 4 hours. Airway inflammation worsened at 4 hours, with increased %neutrophils and TLR4 expression. In addition, bronchodilator responses were suppressed at 4 hours post meal. The high fat meal was equivalent to a large fast food burger with fries. Many individuals, particularly the obese, regularly consume similar meals. This study suggests that following such a meal, asthmatics experiencing bronchoconstriction would not gain optimal relief from their rescue medication.
D. Eating plan for healthy lungs in the obese

Reduce:
- Saturated fat and sodium, eg processed and takeaway foods

Increase:
- Antioxidants and fibre, eg fresh foods such as fruit, vegetables and wholegrains
- Omega-3 fatty acids, eg foods such as fatty fish and fortified dairy products
- Calcium, with consumption of 3-4 serves of calcium per day (especially important in COPD to counteract effects of corticosteroids and smoking on bone mineral density.)

Conclusion
Obesity complicates asthma and COPD management. The effect of weight loss interventions in COPD is not known and given the observed association between high BMI and increased survival in COPD, research in this area is urgently needed. In asthma, the beneficial effects of weight loss are very well described, including improvements in lung function, symptoms and quality of life. Both bariatric surgery and lifestyle interventions can be used to achieve these effects, however, bariatric surgery is only indicated in the morbidly obese. Diet quality is also important in the management of obese asthma, as obesogenic diets which are high in saturated fat and low in antioxidants and fibre, contribute to airway inflammation. A high fruit and vegetable diet and reduced intake of processed/fast foods is recommended. Nutritional status is important in managing obese individuals with airways disease, so should not be ignored.

References

Evaluation
1. Which of the following is not a feature of obese COPD?
   a. Decreased ERV and FRC
   b. Increased use of inhaled medications
   c. Decreased 6 minute walking distance
   d. Decreased peak cycle exercise capacity
2. Which of the following statements are true?
   a. Bariatric surgery is a suitable approach for all obese asthmatics.
   b. Bariatric surgery is only suitable for obese asthmatics if combined with pharmacotherapy.
   c. A 5-10% weight loss will improve quality of life and asthma control in the majority of asthmatics.
   d. Lifestyle interventions are not useful in asthma because the degree of weight loss is inadequate to improve asthma outcomes.

3. A healthy eating plan for obese respiratory patients should be:
   a. High in antioxidants
   b. High in fibre
   c. Low in saturated fat
   d. All of the above

   Please find all correct answers at the back of your handout materials
Treatment options for the obese patient

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Introduction

AIMS

• Aim 1 – To consider the evidence surrounding the use of weight loss interventions in COPD and asthma.

• Aim 2 - To consider suitable approaches to weight loss in COPD and asthma.

• Aim 3 – To review the role of diet quality in COPD and asthma.

OUTLINE

1. Obesity and chronic disease
2. COPD
   a) Effects of obesity
   b) Management of obesity
3. Asthma
   a) Effects of obesity
   b) Management of obesity
4. Diet Quality
   a) Antioxidants
   b) Fibre
   c) Dietary fat
   d) Eating plan for healthy lungs in the obese
1. OBESITY AND CHRONIC DISEASE

**OBESITY PREVALENCE**

"The global epidemic of overweight and obesity - "globesity" - is rapidly becoming a major public health problem in many parts of the world. Paradoxically coexisting with undernutrition in developing countries, the increasing prevalence of overweight and obesity is associated with many diet-related chronic diseases including diabetes mellitus, cardiovascular disease, stroke, hypertension and certain cancers."

(WHO Global database on Body Mass Index)

**HEALTH RISKS ASSOCIATED WITH OBESITY**

- Diabetes
- Hypertension
- Cardiovascular disease
- Metabolic syndrome
  - High blood pressure
  - High blood glucose
  - High blood triglycerides
  - Low HDL cholesterol
  - High waist circumference
- Sleep apnea
- Osteoarthritis
- Some cancers
- Gallbladder disease
- Kidney disease
- Asthma
- Complications in pregnancy/surgery
Obesity-induced inflammation increases risk of chronic inflammatory diseases eg CVD, diabetes, asthma

2A. COPD: EFFECTS OF OBESITY

Obesity prevalence estimates in COPD vary:
18% (Netherlands, Steuten) – 54% (USA, Eliner)
Obesity complicates COPD management:

- ENB and FRC
- Inhaled medications
- Dyspnoea
- Fatigue
- Health related - QOL
- Weight bearing exercise capacity
- No change
- Peak cycle exercise capacity

EFFECTS OF OBESITY ON COPD PROGNOSIS: THE OBESITY PARADOX

Obesity is associated with increased survival in COPD

EFFECTS OF OBESITY ON COPD PROGNOSIS: BY COPD STAGE

BMI and survival differ significantly with stage of COPD.

Mild and mod COPD: non-significant U-shaped relationship, with the lowest risk occurring in normal-weight to overweight subjects.

Severe COPD: mortality continues to decrease with increasing BMI.

OBESITY & INFLAMMATION IN COPD

Obesity - causes systemic inflammation in COPD - likely to contribute to comorbidities: eg CVD, diabetes
HOW COULD OBESITY BE PROTECTIVE?

Obesity increases SI in COPD (↑ FM)

BUT

Obesity also increases FFM
- Overnutrition (increased protein + micronutrients)
- Increased weight bearing
also
Obesity reduces static lung volumes

Different features important at different disease stages???

(poulain et al. chron resp dis 2008)

OBESITY: IMPACT VARIES WITH DISEASE STAGE?

GOLD STAGE 0-2:
Long term effects of obesity important:
- Increased fat mass
- Systemic inflammation
  - Insulin resistance
- Comorbidities:
  CVD, diabetes

GOLD STAGE 3-4:
Short term effects of obesity important:
- Increased fat free mass
- Maintain muscle function
- Reduce risk of death

- Management implications?
  - No studies, so research urgently needed

2B. COPD: MANAGEMENT OF OBESITY
WEIGHT LOSS IN COPD

- Considering known protective effect of FFM in COPD, weight loss should be approached with caution.
- Weight loss, via calorie restriction alone, will lead to FFM loss → Weight loss study underway

WEIGHT LOSS STRATEGY UNDER EVALUATION

Three components:

1. Calorie restriction: reduce intake of nutrient-poor foods (those high in saturated fat and refined carbohydrates, eg take away foods) and replace with nutrient-rich foods (lean protein, fruit, vegetables).
2. High protein: (1.2-1.5g protein per kg ideal body weight): protein intake may be boosted using easily accessible foods, e.g. skim milk powder, custard, milkshakes, eggs, or oral supplement.
3. Resistance training: dietary restriction alone leads to loss of muscle mass, as well as fat mass, so MUST be done in combination with increased physical activity and adequate protein intake, to ensure muscle mass is maintained. Increased protein intake, combined with increased physical activity, will encourage the development of muscle mass, whilst calorie restriction will facilitate loss of fat mass.

EFFECT OF OBESITY ON COPD PULMONARY REHABILITATION OUTCOMES

- Obesity and overweight did not diminish responses
- Rehab programmes may provide suitable vehicle for implementing weight loss interventions

(Sava et al, BMC Pulm Med 2010)
SMOKING CESSATION AND OBESITY

Smoking cessation and weight management/loss can be difficult to undertake at the same time, as both require a lot of effort and commitment. Smoking cessation is often linked with weight gain and is often a serious concern for smokers.

Why do people gain weight when they quit smoking?
- Nicotine withdrawal: Nicotine increases metabolism and after quitting smoking the metabolism slows down.
- Increased appetite: Smoking cessation often leads to increased appetite, which will eventually return to normal.
- Replacing the smoking with food: Increased food intake may occur if food replaces the smoking habit.

Advise patients: Continued smoking has worse effects than a small weight gain. You would need to gain > 40kgs above your recommended weight to equal the same risk of heart disease posed by smoking.

SUMMARY: WEIGHT LOSS IN COPD

- Effects of weight loss in obese COPD patients are unknown. No recommendations currently available.
- Considering the improved prognosis for COPD patients with increasing BMI, weight loss strategies need to be considered with caution.
- A weight loss study, combining calorie reduction, high protein intake and resistance training, is underway.
- COPD pulmonary rehabilitation programmes, involving exercise training and nutritional counselling, provide an opportunity for administering weight loss interventions, but have no proven efficacy in achieving weight loss.
- Other strategies for achieving weight loss: eg pharmacotherapy or bariatric surgery also not tested in COPD.

3A. ASTHMA: EFFECTS OF OBESITY
3B. ASTHMA: MANAGEMENT OF OBESITY

WEIGHT LOSS TREATMENT OPTIONS

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>Treatment</th>
<th>Diet, physical activity, and behavior therapy</th>
<th>Pharmacotherapy</th>
<th>Surgery</th>
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<td>18-24.9</td>
<td>With caution</td>
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<td>Yes</td>
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<tr>
<td>25-29.9</td>
<td>With caution</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
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<td>30-34.9</td>
<td>With caution</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>≥ 35</td>
<td>With caution</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
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</tbody>
</table>

(National Institute of Health)
Option 1: Bariatric Surgery

Many studies show improvements in asthma outcomes following bariatric surgery:

- **Follow-up**: 1-7.3 yrs
- **Weight loss**: 5.4-20.3 kg/m²
- **Outcomes**: improved lung function, symptoms & medication use

Overall, clear improvements in asthma. But, not indicated for majority of overweight and obese asthmatics. (>BMI 35 or 40 kg/m²)

**NIH Guidelines for Patient Selection for Bariatric Surgery**

- >100 lb. excess weight
- BMI <40 kg/m² without obesity-associated comorbidities (e.g., diabetes, cardiovascular disease, arthritis, obstructive sleep apnea)
- BMI 30-39.9 kg/m² with 1 or more associated medical problems
- Previous failed weight-loss attempts (e.g., nonsurgical interventions: diet control, behavioral modification, exercise)

**WEIGHT LOSS TREATMENT OPTIONS IN ASTHMA**

Option 2: Lifestyle Intervention: Calorie restriction

*Non-randomised dietary restriction studies:*

- **Intervention period**: 6-14wks
- **Weight loss**: 8-14.5%
- **Outcomes**: improved lung function, symptoms & QoL

**Two published RCTs:**

   - Control Group: n=19, mean weight loss of 0.3%
   - Intervention group: n=19, mean weight loss of 14.5%
   - FEV1 improved by 7.2%, FVC improved by 8.6%
   - During 12 month follow-up, fewer asthma exacerbations

2. Scott et al (2012): see over

**Screening Visit**

(to determine eligibility)

**Randomisation:**

- Diet
- Exercise
- Diet + Exercise

**Week 0 Visit**

**Intervention Phase**

(10 weeks)

**Week 10 Visit**

(Scott et al. Clin Exp Allergy, 2012)

**Aim:** To examine the effect of body fat reduction on clinical outcomes in overweight and obese asthmatics.

**Inclusion Criteria**

Dr’s diagnosis of asthma
History of AHR
18+ years
BMI 28-40kg/m²
Non-smoker
71 Participants Screened

Diet n=17
Total of ~4500 kJ / day
Meal replacements: 2 meals/day
Main meal of choice (1/day) + snacks
Weekly dietetics counselling
Weekly steps increased by 10% /week to 10,000 steps

Exercise (n=14)
12-week gym membership
Personal trainer: 1 hr / week
Additional 2 sessions/week in own time

Combined (n=14)
Diet + exercise

2 withdrawals
4 withdrawals
1 withdrawal

Weight, fat and muscle mass loss

Weight loss associated with improved ERV, and Asthma Control and QoL

Asthma Quality of Life
Summary of weight loss in asthma

- Obesity complicates asthma management.
- Bariatric surgery improves asthma in the morbidly obese.
- Effects of pharmacotherapy unknown.
- Diet and exercise intervention is effective in improving asthma outcomes in overweight and mild-moderately obese subjects.
- Dietary restriction is more effective at achieving weight loss than exercise alone.
- Even a small amount of weight loss can improve asthma outcomes.
- 5-10% weight loss should be advocated
  - Realistic goal – dietetic input important
  - Clinically improved QoL in 83% of patients and ACQ in 58% of patients

4. DIET QUALITY

OBESITY AND DIET QUALITY

The obesogenic diet features:
- MACRONUTRIENT SURPLUS
- ‘FAST’ or PROCESSED FOODS
- LOW IN FRUIT AND VEGETABLES
- LOW IN WHOLE GRAINS

Diet Quality

DIETARY FAT

ANTIOXIDANTS

FIBRE
4A. ANTIOXIDANTS

ANTIOXIDANTS AND INFLAMMATION

Activated inflammatory cells in asthma – antioxidant therapy?

OXIDATIVE STRESS INCREASED IN COPD

(Montuschi, AJRCCM, 2000)
### MORGEN Study

<table>
<thead>
<tr>
<th>Diet in polyphenols/bioflavanoids (catechin, flavonol, and flavone) (58mg/day)</th>
<th>Effect on FEV1 and symptoms</th>
<th>Protective against FEV1 decline</th>
<th>Protective against onset of symptoms; chronic cough and breathlessness</th>
<th>(Tabak et al. 2001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet rich in fruits, vegetables, and fish intake</td>
<td>Effect on 20-year COPD mortality</td>
<td>24% lower COPD mortality risk.</td>
<td>(Walda et al. 2002)</td>
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</tr>
</tbody>
</table>

### European countries (Finnish, Italian and Dutch) cohort

Diet rich in fruits, vegetables, and fish intake

Effect on 20-year COPD mortality

24% lower COPD mortality risk.

(Walda et al. 2002)

---

### OXIDATIVE STRESS INCREASED IN ASTHMA

(Wood et al., AJRCCM, 2005)

---

### ANTIOXIDANT DEFENCES IMPAIRED IN ASTHMA

(Wood et al., J Am Col Nutr, 2005)

Plasma carotenoids reduced in asthma despite no differences in dietary intake, suggested increased utilisation due to increased oxidative burden.
Following 10 days on a low antioxidant diet, sputum %neutrophils increased, lung function and asthma control worsened. N = 22 stable asthmatics

N=136 asthmatics
RCT: High F&V diet (≥ 5 serves vegetables, ≥ 2 serves fruit) vs Low F&V diet (≤ 2 serves vegetables, ≤ 1 serve fruit)

Kaplan Meier survival curve for time to exacerbation

One proportional hazards model: Subjects on low F&V diet were 2.3 times more likely to exacerbate (p=0.038)


4B. FIBRE
Dietary fibre (soluble fibre):
- Fermented by bacteria in the gut to produce short chain fatty acids (SCFA)
- SCFA activate GPR43
- Anti-inflammatory mediators produced

Low fibre diet leads to loss of GPR43 activity – reduction in anti-inflammatory mediators

(Modified from Li et al, Nature, 2010)

GPR43 deficiency:
- BAL cell counts and EPO activity increased (Maslowski, Nature, 2009)

Total dietary fibre was negatively associated with COPD risk:
highest vs lowest intake, relative risk = 0.67 (CI 0.5, 0.9), p=0.03
**ERS**

**FIBRE AND ASTHMA**

Multiple linear regression of dietary intake as predictors of lung function in asthma: Fibre intake positively predicted lung function and eosinophilic airway inflammation. Fat negatively predicted airway eosinophilia.

---

**FEV1 (L)  FVC (L)  FEV1/FVC  %Eosinophils**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Coefficient</th>
<th>(p value)</th>
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<th>(p value)</th>
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</thead>
<tbody>
<tr>
<td>Fibre intake</td>
<td>0.02 (0.001)**</td>
<td>0.02 (0.001)**</td>
<td>-0.004 (0.476)</td>
<td>-0.36 (0.026)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat intake</td>
<td>-0.04 (0.311)</td>
<td>-0.05 (0.451)</td>
<td>-0.004 (0.476)</td>
<td>-0.18 (0.019)**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.01 (0.001)</td>
<td>-0.01 (0.001)</td>
<td>0.001 (0.139)</td>
<td>0.50 (0.092)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>-0.71 (0.01)</td>
<td>-2.13 (0.001)</td>
<td>0.056 (0.085)</td>
<td>-0.22 (0.027)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>-0.04 (0.309)</td>
<td>-0.02 (0.026)</td>
<td>0.003 (0.013)</td>
<td>0.24 (0.022)</td>
<td></td>
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</tr>
</tbody>
</table>

*(Berthon et al, Respirology)*

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**4C. DIETARY FAT**

**DIETARY FAT AND %FEV1**

**Method:**
Participants recruited from Hunter Community Study
- n = 198, aged between 55 and 85 years
- Risk factors for lung function decline

**Key results:**
Negative predictors of lung function (FEV1) included:
- %Dietary fat (effect was similar in magnitude to former smoking)

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FATTY ACIDS AND INFLAMMATION

- Anti-inflammatory fatty acids:
  - Omega-3
  - Monounsaturated

- Pro-inflammatory fatty acids:
  - Saturated
  - Trans
  - Omega-6

Increased cytokine expression

Hotamisligil, 2008
**DIETARY FAT CHALLENGE**

- Stable asthmatics (n=51): fasted, medications withheld
- High or low fat meal then bronchodilator
- Airway inflammation and lung function assessed at 0, 4 hrs

![Image of meal options: High Fat Meal (2 hash browns, sausage & egg muffin, sausage muffin) and Low Fat Meal (yoghurt)]

**DIETARY FAT AND AIRWAY INFLAMMATION AT 4 HRS**

- Subjects who consumed the High Fat meal had an increase in airway inflammation (sputum % neutrophils and TLR4 expression).

![Graph showing increase in neutrophils and eosinophils with High Fat meal compared to Low Fat meal]

**DIETARY FAT AND BRONCHODILATION AT 4 HRS**

- Subjects who consumed the High Fat meal had reduced bronchodilator response

![Graph showing reduced bronchodilator response with High Fat meal compared to Low Fat meal]
**4D. EATING PLAN FOR HEALTHY LUNGS IN THE OBESE**

**REDUCE:**
- Saturated fat and sodium, eg processed and takeaway foods

**INCREASE:**
- Antioxidants and fibre, eg fresh foods such as fruit and vegetables
- Omega-3 fatty acids, eg foods such as fatty fish and fortified dairy products
- Calcium, with consumption of 3-4 serves of calcium per day (especially important in COPD to counteract effects of corticosteroids and smoking on bone mineral density.)

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**Summary and Conclusion**

Obesity complicates asthma and COPD management

**Weight loss:**
- **COPD:** Evidence not available
- **Asthma:** Weight loss (via bariatric surgery/ lifestyle interventions) improves lung function, QoL, symptoms

**Diet Quality:**
- Obesogenic diet contributes to airway inflammation.
  - High fruit and vegetable diet recommended
    - Antioxidants: modify airway inflammation/ lung function in asthma, protect against lung function decline and COPD onset.
    - Fibre: reduces airway inflammation (?), reduces asthma and COPD risk.
  - Reduced intake of processed/ fast foods recommended
    - High saturated fat intake associated with worse lung function and airway inflammation in asthma.

*NUTRITIONAL STATUS IS IMPORTANT IN AIRWAYS DISEASE!*
Faculty Disclosures

There are no faculty disclosures for this course.
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Answers to submitted MCQ’s

Please find all correct answers in bold below

Complications of obesity in the COPD patient – Prof. Emiel F. M. Wouters

1. Obesity has important effects on respiratory mechanics. One of the following statements is correct:
   a. Obesity increases ERV
   b. Obesity decreases TLC
   c. Obesity decreases FRC.

2. Obesity has important effects on exercise capacity. One of the following statements is correct:
   a. Obese patients do not experience greater exercise limitation than normal weight patients during peak cycle ergometry.
   b. Operating lung volumes are not modified by obesity in COPD.
   c. Six minute walk is unaffected by obesity in COPD.

3. Systemic inflammation is a characteristic finding in COPD. One of the following statements is correct:
   a. Systemic inflammation in COPD is present in all COPD patients.
   b. Systemic inflammation in COPD is characterised by raised IL-8.
   c. Systemic inflammation in COPD is characterised by raised CRP and fibrinogen.

Sleep apnoea and the obesity-hypoventilation syndrome – Dr. Fernando Masa

1. What is true with regard to treatment with CPAP?
   a. Reduction of blood pressure is about 10 mmHg
   b. In general, patients with higher AHI have a similar decrease in blood pressure as for patients with low IAH.
   c. BMI does not influence blood pressure lowering
   d. The benefit depends upon compliance with CPAP.

2. What is false about how acts noninvasive ventilation?
   a. Unloading the respiratory muscles decreasing its chronic fatigue
   b. During sleep decreases or prevents alveolar hypoventilation (especially in the REM period) but not obstructive events.
   c. Prevents the elevation of PaCO2 and bicarbonate which cause a "blunting" of the respiratory center and hypercapnia.

3. Which treatment is believed to be the least effective for obesity hypoventilation syndrome?
   a. Weight loss by diet.
   b. Noninvasive intermittent mechanical ventilation
   c. CPAP.
   d. Medroxyprogesterone.

4. How is the diagnosis of obesity hypoventilation syndrome performed?
   a. Patients with sleep apnea and daytime hypercapnia regardless the presence of obesity and sleep apnea degrees.
   b. Patients with obesity (BMI>30), daytime hypercapnia (PCO2>45 mmHg) and sleep disorders when other diseases potentially causing hypercapnia have been excluded.
   c. Patients with obesity (BMI>30), daytime hypercapnia (PCO2>45 mmHg) and sleep apnea (AHI>30) without be necessary to considered other potently causes of daytime hypercapnia.
   d. Patients with obesity (BMI>30), severe sleep apnea (AHI>50) and nocturnal hypoventilation without daytime hypercapnia.
Treatment options for the obese patient – Dr. Lisa G. Wood

1. Which of the following is not a feature of obese COPD?
   a. Decreased ERV and FRC
   b. Increased use of inhaled medications
   c. Decreased 6 minute walking distance
   d. Decreased peak cycle exercise capacity

2. Which of the following statements are true?
   a. Bariatric surgery is a suitable approach for all obese asthmatics.
   b. Bariatric surgery is only suitable for obese asthmatics if combined with pharmacotherapy.
   c. A 5-10% weight loss will improve quality of life and asthma control in the majority of asthmatics.
   d. Lifestyle interventions are not useful in asthma because the degree of weight loss is inadequate to improve asthma outcomes.

3. A healthy eating plan for obese respiratory patients should be:
   a. High in antioxidants
   b. High in fibre
   c. Low in saturated fat
   d. All of the above