COPD and obesity

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## Disclosure belangen spreker

<table>
<thead>
<tr>
<th>(potentiële) belangenverstrengeling</th>
<th>Frits Franssen</th>
</tr>
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<tbody>
<tr>
<td>Voor bijeenkomst mogelijk relevante relaties met bedrijven</td>
<td>AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Mundipharma, Novartis, TEVA</td>
</tr>
</tbody>
</table>

- Sponsoring of onderzoeksgeld
- Honorarium of andere (financiële) vergoeding
- Aandeelhouder
- Andere relatie, namelijk ...
COPD and obesity: agenda

1) Epidemiology
2) Impact of obesity on
   * Diagnosis and treatment
   * Symptoms
   * Lung function
   * Exercise capacity
   * Clinical phenotypes
   * Prognosis
3) How to manage the obese COPD patient
4) Summary and discussion
‘Globesity’

Obesity (BMI > 30 kg·m$^{-2}$) is a 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, 2014*
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=18,606)

Adjusted risk of obesity was 22% lower in COPD

Vanfleteren et al., Chron Respir Dis 2016
Obesity is a risk factor for dyspnea

Sin et al., NHANES III, Arch Intern Med 2002
Obesity is a risk factor for misdiagnosis of COPD

52% of patients (n=5,493) with a clinical COPD diagnosis had chronic airflow limitation

The proportion of patients with chronic airflow limitation decreased as BMI increased

Collins et al., Chest 2014
Obesity is a risk factor for overtreatment of COPD

Among subjects without chronic airflow limitation, overweight and obese subjects were less likely to have therapy de-escalated or remain off therapy.

Health care professionals are currently missing potential opportunities to recognize and treat other causes of dyspnea.

Collins et al., Chest 2014; Franssen FM, Chest 2014
COPD and obesity: symptoms and health status

Dyspnea

- Mild dyspnea (MRC 1)
- Moderate dyspnea (MRC 2-3)
- Severe dyspnea (MRC 4-5)

Proportion of patients (%)

Health status

- SGRQ Symptoms
- SGRQ Activity
- SGRQ Impact
- SGRQ Total

Proportion of patients (%)

Cecere et al., COPD 2011
Normal lung volumes

- Maximum possible inspiration
- Inspiratory reserve volume
- Vital capacity
- Inspiratory capacity
- Tidal volume
- Total lung capacity
- Maximum voluntary expiration
- Residual volume
- Functional residual capacity
Static and dynamic hyperinflation in COPD

- Static Hyperinflation:
  - Air trapping at rest: „Years - Decades“

- Dynamic Hyperinflation:
  - Air trapping from exertion: „Seconds – Minutes“
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?

Lean

Obese

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
Obese COPD patients do not experience greater exercise limitation and dyspnea than normal weight patients during peak cycle ergometry.
Effects of obesity on weight-bearing vs. weight-supported exercise testing in COPD

In contrast to cycle ergometry, six minute walking distance is shorter in obese COPD patients compared with non-obese patients, matched for gender, age and FEV$_1$

Maatman et al., Respirology 2016
Combined effects of obesity and COPD: systemic consequences

Fabbri et al., Eur Respir J 2008
Frequencies of objectively identified comorbidities

- Anemia: 5%
- Myocardial Infarction: 9%
- Underweight: 14%
- Depression: 16%
- Anxiety: 21%
- Renal Impairment: 22%
- Obesity: 23%
- Muscle Wasting: 28%
- Osteoporosis: 31%
- Dyslipidemia: 36%
- Hypertension: 48%
- Atherosclerosis: 53%
- Hyperglycemia: 54%

Vanfleteren et al., Am J Respir Crit Care Med 2013
Clustering of objectively identified comorbidities in COPD

<table>
<thead>
<tr>
<th></th>
<th>% Renal Impairment</th>
<th>% Anemia</th>
<th>% Hypertension</th>
<th>% Obesity</th>
<th>% Underweight</th>
<th>% Hyperglycemia</th>
<th>% Dyslipidemia</th>
<th>% Osteoporosis</th>
<th>% Anxiety</th>
<th>% Depression</th>
<th>% Atherosclerosis</th>
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<tr>
<td>Obesity</td>
<td>8</td>
<td>8</td>
<td>56</td>
<td>0</td>
<td>0</td>
<td>72</td>
<td>42</td>
<td>18</td>
<td>12</td>
<td>18</td>
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<tr>
<td>Underweight</td>
<td>50</td>
<td>3</td>
<td>40</td>
<td>0</td>
<td>93</td>
<td>37</td>
<td>27</td>
<td>57</td>
<td>21</td>
<td>4</td>
<td>17</td>
<td>3</td>
</tr>
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</table>

Body composition is an important discriminating factor in unbiased clustering of COPD

Vanleteren et al., Am J Respir Crit Care Med 2013
Classical COPD phenotypes revisited

**Cachectic phenotype**
- Emphysema
- Underweight
- Low muscle mass
- Fibre type shift I > II
- Osteoporosis

**Metabolic phenotype**
- Atherosclerosis
- Overweight
- Low fat mass
- High fat mass
- Bronchial wall thickening

ERS Taskforce ‘Nutrition in COPD’, Eur Respir J 2014
Assessing low fat-free mass: the impact of aging and BMI

Above the age of 60, fat-free mass index declines

Fat-free mass index is positively correlated with BMI

There is a rationale for gender-, age- and BMI specific cut-offs

Kyle et al., Nutrition 2003
New reference values for fat-free mass index: results from the UK Biobank (n = 186,975)

<table>
<thead>
<tr>
<th>Age, y</th>
<th>BMI, kg/m²</th>
<th>Men</th>
<th></th>
<th></th>
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<th>Women</th>
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<td>P10</td>
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<td>45–59</td>
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<td>14.9</td>
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<td></td>
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<td>17.0</td>
<td>17.5</td>
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<td></td>
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<td>19.3</td>
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<td></td>
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<td>20.9</td>
<td>21.3</td>
<td>21.8</td>
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<td>60–69</td>
<td>&lt;18.50</td>
<td>14.5</td>
<td>14.9</td>
<td>15.2</td>
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<td>13.0</td>
<td>13.6</td>
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<td>20.4</td>
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<td>16.7</td>
<td>17.0</td>
<td>17.5</td>
<td>18.1</td>
</tr>
</tbody>
</table>

Body composition data from the general population indicate that in overweight and obese populations higher cut-off values for low fat-free mass should be applied.
The prevalence of low muscle mass in overweight and obese COPD patients

A large proportion of overweight and obese patients with COPD fulfill the new criteria for low fat-free mass

Franssen et al., in preparation
Combined effects of obesity and COPD: obesity paradox

Landbo et al., Am J Respir Crit Care Med 1999
Causes of death in COPD

Only a minority of COPD patients die from this disease

Mannino et al., Respir Med 2006
30% of patients do not have systemic inflammation, whereas only 16% have persistent systemic inflammation.

Age, high BMI, current smoking, poor health status and airflow limitation were independent risk factors for persistent systemic inflammation.

Agusti et al., PloS One 2012
Adipocyte dysfunction, systemic inflammation and cardiovascular risk

Van Gaal et al., Nature 2006
Excessive visceral fat accumulation in COPD

OLD subjects had increased plasma IL-6, adiponectin and PAI-1. IL-6 was an independent predictor for cardiovascular mortality.

van den Borst et al., Am J Respir Crit Care Med 2013
Considerations for treatment of obesity in COPD

**PRO:**
- Increased dyspnea at rest
- Reduce cardiovascular risk
- Improve physical functioning
- Reduce mortality in non-severe COPD
- Improve glucocorticosteroid responsiveness

**CON:**
- Reduced static lung volumes
- Preserved non-weight bearing exercise tolerance
- Comparable exercise-related symptoms
- Lower prevalence of muscle wasting
- Lower prevalence of reduced bone mineral density
- Better prognosis in severe COPD
Management of obesity in COPD

WHY?
- CV risk factors?
- Comorbidities?
- Symptoms?
- Performance?
- Mortality?

HOW?
- VLCD?
- Activity?
- Surgery?
- Drugs?

NO STUDIES IN COPD
Multidimensional treatment of adult obesity

Initial goal: loss of 10% of baseline weight after six months at a rate of 0.5 - 1.0 kg per week

Treating obesity in COPD

Inclusion: COPD, BMI > 30 kg/m², FEV₁ < 80%, clinically stable

Exclusion: Current smoking, cardiac disease, insulin users, significant orthopaedic problems

Program: - Low-energy diet, 2 meal replacements, high-protein intake
- Home-based strength training 3 days/week
- Two weekly treatment visit, two weekly phone call
- 12 weeks
Treating obesity in COPD

(a) BMI

(b) Percent body fat

(c) Skeletal Muscle Mass - BIA

(d) Appendicular Skeletal Muscle Mass Index

-6.4 kg

*p<0.0001

p=0.39

p=0.2

McDonald et al., Respirology 2016
Treating obesity in COPD

(a) SGRQ

(b) 6MWD

(c) BODE Index

(d) Strength - Shoulder Abduction

McDonald et al., Respirology 2016
# Treating obesity in COPD

<table>
<thead>
<tr>
<th>Pulmonary function</th>
<th>n</th>
<th>Pre</th>
<th>Post</th>
<th>p value</th>
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<tbody>
<tr>
<td>Post-bronchodilator FEV1 (L), mean (SD)</td>
<td>28</td>
<td>1.7 (0.5)</td>
<td>1.8 (0.5)</td>
<td>0.4112</td>
</tr>
<tr>
<td>Post-bronchodilator FVC (L), mean (SD)</td>
<td>28</td>
<td>2.8 (0.8)</td>
<td>3.0 (0.8)</td>
<td>0.0033</td>
</tr>
<tr>
<td>FEV1/FVC ratio, mean (SD)</td>
<td>28</td>
<td>61.7 (12.6)</td>
<td>60.4 (13.2)</td>
<td>0.1886</td>
</tr>
<tr>
<td>Functional residual capacity (L), mean (SD)</td>
<td>14</td>
<td>3.4 (1.1)</td>
<td>3.5 (1.0)</td>
<td>0.19</td>
</tr>
<tr>
<td>Residual volume (L), mean (SD)</td>
<td>14</td>
<td>2.5 (0.9)</td>
<td>2.4 (0.8)</td>
<td>0.42</td>
</tr>
<tr>
<td>End residual volume (L), mean (SD)</td>
<td>14</td>
<td>0.95 (0.4)</td>
<td>1.1 (0.5)</td>
<td>0.15</td>
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<tr>
<td>Total lung capacity (L), mean (SD)</td>
<td>14</td>
<td>5.6 (1.3)</td>
<td>5.7 (1.4)</td>
<td>0.27</td>
</tr>
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</table>
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
The impact of exercise modality on physiological responses and dyspnea in obese COPD patients

Compared with cycling, treadmill walking is associated with higher oxygen uptake and greater desaturation in obese COPD patients

Ciavaglia et al., Eur Respir J 2014
The impact of exercise modality on physiological responses and dyspnea in obese COPD patients

Operating lung volumes are similar cycling and treadmill walking in obese patients with COPD

Ciavaglia et al., Eur Respir J 2014
The impact of exercise modality on physiological responses and dyspnea in obese COPD patients

Exercise modality has no effect on dyspnea/work rate or dyspnea/ventilation relationships in obese patients with COPD

Ciavaglia et al., Eur Respir J 2014
Special considerations for pulmonary rehabilitation in patients with COPD and obesity

Water-based exercise training was more effective than land-based exercise training in increasing exercise capacity and health status in COPD patients and co-morbidities (42% obesity)

McNamara et al., Eur Respir J 2012
COPD and obesity: summary

1) The number of COPD patients with obesity is expected to increase, in line with the obesity pandemic.

2) For accurate clinical assessment and disease management it is essential to understand the effects of excessive fat mass in patients in which COPD and obesity collide.

3) Contrary to expectations, obesity is not necessarily associated with worse patient-related outcomes in COPD.

4) The role of adipose tissue dysfunction in COPD pathophysiology and increased cardiovascular risk is a hot research topic.

5) The effects of weight loss and the optimal BMI for obese patients with COPD are currently unknown.

6) The presence of comorbid obesity in a patient with COPD may warrant specific programme adaptations during pulmonary rehabilitation.

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