Obesity in COPD:
to treat or not to treat?

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Background

• **COPD**
  - 3rd leading cause of mortality worldwide
  - 2nd leading cause of hospital admission in Australia

• **Overweight and obesity**
  - Estimated 5th leading cause of death worldwide
  - (~ 208 million adults that die each year as a result of overweight or obesity)
  - The worldwide prevalence of obesity has nearly doubled since 1980.
  - In 2008, more than 1.4 billion adults (35%) around the world were considered overweight, and of these over 200 million (11%) adults were classified as obese.
COPD Phenotypes

Pink Puffer
Obesity in COPD is common

COPD is a complex multi system disease associated with multiple comorbidities and clinical problems.

- Resulting in poor health status, frequent exacerbations and decreased physical activity.
Obesity

- Obesity is associated with increased mortality and multiple comorbidities
- Associated with reduced health status and physical inactivity
Obese COPD

- COPD itself has a major adverse impact on patients’ exercise capacity, health status and mortality.
- When obesity and COPD co-exist patients suffer an additional burden
  - a further reduction in exercise capacity,
  - are less active,
  - have poorer health status
Obesity Paradox

• Obesity - an established risk factor for poor outcome
• Paradoxically in COPD mild to moderate obesity is associated with improved survival, improved lung function and reduced hospital admission.

Schols AM et al. AJRCCM 1998; 157: 1791-7
# Results reproduced in many studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample</th>
<th>Length of followup</th>
<th>Primary outcome</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Landbo et al</td>
<td>Prospective cohort (the Copenhagen City Heart Study)</td>
<td>1,218 men and 914 women ages 21-89 years with airway obstruction (FEV1:FVC ratio &lt;0.70)</td>
<td>17 years</td>
<td>Mortality from COPD and all causes</td>
<td>In severe COPD, all-cause mortality decreased as BMI increased (RR 0.62. 95% CI 0.41-0.94; ( P&lt;0.001 ) from BMI &gt;30 compared to BMI of 20-24.9)</td>
</tr>
<tr>
<td>Jee et al</td>
<td>Prospective cohort</td>
<td>1,213,829 Koreans aged 30-95 years</td>
<td>12 years</td>
<td>Body weight and risk of death</td>
<td>The risk of death from respiratory causes decreased progressively with increasing BMI: however, too few subjects had a BMI above 30 for evaluation of obesity</td>
</tr>
<tr>
<td>Hallin et al</td>
<td>Prospective multicenter study</td>
<td>261 hospitalised patients with COPD</td>
<td>2 years after hosp</td>
<td>Mortality</td>
<td>Lowest mortality was in overweight patients (BMI 25-30)</td>
</tr>
<tr>
<td>McGhan et al</td>
<td>Prospective cohort</td>
<td>51,353 patients who were discharged after an exacerbation of COPD in the VA health care system</td>
<td>5 years</td>
<td>Rates of rehosp for COPD and death from all causes</td>
<td>Obesity was associated with a reduction in the risk of death (HR 0.76, 95% CI 0.70-0.82)</td>
</tr>
<tr>
<td>Lainscak et al</td>
<td>Retrospective chart review</td>
<td>968 patients hosp due to AECOPD</td>
<td>3.26 years</td>
<td>Mortality and acute exacerbation of COPD</td>
<td>Higher BMI was independently predictive of survival, with each unit increase in BMI associated with 5% lower chance of death. Optimal BMI was in the overweight category</td>
</tr>
<tr>
<td>Cao et al</td>
<td>Meta-analysis</td>
<td>Included 22 studies comprising 21,150 participants with COPD</td>
<td>NA</td>
<td>Mortality</td>
<td>Overweight (RR 0.47, 95% CI 0.33-0.68) and obesity (RR 0.59, 95% CI 0.38-0.91) was associated with lower mortality</td>
</tr>
<tr>
<td>Zapatero et al</td>
<td>Retrospective chart review</td>
<td>313,233 patients admitted with COPD as the primary diagnosis</td>
<td>NA</td>
<td>In hospital mortality and readmission within 30 days</td>
<td>Obese patients showed a lower inhospital mortality risk (OR 0.52, 95%CI 0.49-0.55) when compared to non-obese patients</td>
</tr>
<tr>
<td>Hanson C.</td>
<td>IJCOPD 2014</td>
<td></td>
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</tbody>
</table>
Why?

• Overweight or obese patients with COPD may receive medical attention earlier (ie, while having better preserved expiratory flows and less hyperinflation compared with their lean counterparts).

• Peak oxygen consumption (VO2) is higher in obese patients with COPD than in their normal-BMI counterparts.

• Obese patients with COPD may not only have more adipose tissue, but more muscle, offering a survival advantage.
Is the obesity paradox related to BMI?

Increasing BMI may reflect higher fitness levels, greater metabolic reserve and less cachexia.

BMI – an inappropriate surrogate for adiposity

? may explain the obesity paradox.

Importance of muscle mass

In COPD, sarcopenia adversely affects functional outcomes:

- Muscle strength
- Peak workload
- Cycle endurance
- 6 MWD (in men)

importance of muscle mass

Less sarcopenia in obese COPD compared
Clinical Conundrum

Healthy Weight

- Improved survival
- Reduced hospitalisations
- Better lung function
- Better non weight bearing exercise capacity
- Increased breathlessness
- Reduced quality of life

Obese

- Worse survival
- Increased hospitalisations
- Reduced CVD risk
- Reduced metabolic syndrome
- Reduced DM

In older people weight loss interventions reduces both fat and muscle mass.
Postoperative pulmonary complications are as important as preoperative risk factors in the management of COPD. The principal potential factors contributing to the risk include smoking, poor general health status, age, obesity, and COPD severity. Weight loss interventions have not been tested in COPD to date and no recommendations are currently available.
To treat?  
Or no treats!
NO Evidence
To determine if weight reduction, combined with resistance training to maintain muscle mass, would improve clinical outcomes and reduce inflammation in obese COPD.

Hypothesis

Obese COPD patients dietary restriction and resistance training will result in improved clinical outcomes without reduction in skeletal muscle.
Methods

A before-after clinical trial

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obese (BMI ≥30kg/m²)</td>
<td>• MMSE &lt;24</td>
</tr>
<tr>
<td>Diagnosis with COPD</td>
<td>• Medical condition requiring specialised dietary plan</td>
</tr>
<tr>
<td>Ex-smoker &gt; 6 months</td>
<td>• Significant comorbidity</td>
</tr>
<tr>
<td>Wanting to lose weight</td>
<td>• Orthopaedic problems (contraindication to exercise)</td>
</tr>
<tr>
<td></td>
<td>• Change in weight (±5%) in the last 3/12</td>
</tr>
</tbody>
</table>
Intervention

Participants (n=28) received:

- a 12 week weight reduction programme
  - Meal replacements (2 meals per day) plus one additional meal with snacks (3300-5000KJ)
  - protein prescribed at 1.2-1.5g/kg body weight/day
  - dietary counselling by a dietitian

- resistance strength training
  - prescribed and supervised by a physiotherapist.

- participants were reviewed face to face by the dietitian and physiotherapist every two weeks for counselling.
### Participant Flow

- **Assessed for eligibility (n=50)**
  - Excluded (n=17)
    - Not meeting inclusion criteria (n=16)
    - Declined to participate (n=1)

- **Enrolled (n=33)**

- **Completed (n=28)**
  - Withdrawn (n=5)
    - Withdrawn by investigators for excessive ETOH intake while on low KJ diet
  - 1 Lost to follow up
  - 1 Abdominal Pain
  - 2 Too unwell to continue

- **Withdrawn (n=5)**
  - Withdrawn by investigators for excessive ETOH intake while on low KJ diet
## Demographics

### The Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>M</th>
<th>F</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: M/F</td>
<td>17</td>
<td>11</td>
<td>67.6 (6.3)</td>
</tr>
<tr>
<td>Height (cm), mean (SD)</td>
<td></td>
<td></td>
<td>174.1 (7.2)</td>
</tr>
<tr>
<td>Weight (kg), mean (SD)</td>
<td></td>
<td></td>
<td>99.3 (15.1)</td>
</tr>
<tr>
<td>Status – St George Respiratory Questionnaire, mean (SD)</td>
<td></td>
<td></td>
<td>52.3 (15.1)</td>
</tr>
<tr>
<td>Asthma Assessment Test (CAT), mean (SD)</td>
<td></td>
<td></td>
<td>20.1 (7)</td>
</tr>
<tr>
<td>Smoking Pack years, mean (SD)</td>
<td></td>
<td></td>
<td>32.8 (23.0)</td>
</tr>
<tr>
<td>Bronchodilator FEV1 % predicted, mean (SD)</td>
<td></td>
<td></td>
<td>61.6 (17.1)</td>
</tr>
<tr>
<td>Bronchodilator FVC % predicted, mean (SD)</td>
<td></td>
<td></td>
<td>78.6 (20.3)</td>
</tr>
<tr>
<td>Expiratory Ratio</td>
<td></td>
<td></td>
<td>61.6 (13.1)</td>
</tr>
<tr>
<td>Total Residual Capacity (L), mean (SD)</td>
<td></td>
<td></td>
<td>3.4 (1.1)</td>
</tr>
</tbody>
</table>
Weight loss

(a) BMI

(b) Percent body fat

* *p<0.0001
Weight loss

(C) Skeletal Muscle Mass - BIA

(d) Appendicular Skeletal Muscle Mass Index

pre | post
---|---
p=0.39

kg/m²

pre | post
---|---
p=0.2
OPD Outcomes

(a) SGRQ

(b) 6MWD

(c) BODE Index

(d) Strength - Shoulder Abduction
<table>
<thead>
<tr>
<th>Pulmonary function</th>
<th>Pre</th>
<th>Post</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post bronchodilator FEV$_1$(L), mean (SD)</td>
<td>1.7 (0.5)</td>
<td>1.8 (0.5)</td>
<td>0.4</td>
</tr>
<tr>
<td>Post bronchodilator FVC (L), mean (SD)</td>
<td>2.8 (0.8)</td>
<td>3.0 (0.8)</td>
<td>0.003</td>
</tr>
<tr>
<td>FEV1/FVC ratio, mean (SD)</td>
<td>61.7 (12.6)</td>
<td>60.4 (13.2)</td>
<td>0.19</td>
</tr>
<tr>
<td>Functional Residual Capacity (L), mean (SD)</td>
<td>3.4 (1.1)</td>
<td>3.5 (1.0)</td>
<td>0.19</td>
</tr>
<tr>
<td>End Residual Volume (L), mean (SD)</td>
<td>0.95 (0.4)</td>
<td>1.1 (0.5)</td>
<td>0.15</td>
</tr>
<tr>
<td>Residual Volume (L), mean (SD)</td>
<td>2.5 (0.9)</td>
<td>2.4 (0.8)</td>
<td>0.42</td>
</tr>
<tr>
<td>Total Lung Capacity (L), mean (SD)</td>
<td>5.6 (1.3)</td>
<td>5.7 (1.4)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

McDonald VM, Gibson PG, Scott HA, Baines PJ, Hensley MJ, Pretto JJ, Wood LG. Respirology 2016
Conclusions

In obese COPD patients, dietary energy restriction coupled with resistance strength training results in clinically significant improvements in body composition, health status, symptoms and functional capacity.

It did not result in loss of skeletal muscle mass or strength.

This intervention resulted in an improved prognostic score (BODE), but longer term follow up is required.

12 month follow up of pilot participants

McDonald VM, Gibson PG, Scott HA, Baines PJ, Hensley MJ, Pretto JJ, Wood LG. Respirology 2016
Does it help interrelated comorbidities?

**Hypothesis:** A single obesity-targeted intervention involving dietary restriction and resistance exercise training can improve multiple markers of COPD-associated comorbidities in obese COPD.

**Aim:** The aim of this study was to evaluate the changes in markers of comorbidities pre-post intervention.
Does it help interrelated comorbidities?

Improves lipid and metabolic markers, blood pressure and depression score in obese COPD.

Improvements were primarily observed in participants with elevated baseline levels of the respective markers.

Potential for personalized management of comorbidities in obese COPD patients.
Obese COPD

Metabolic Syndrome
Depression
Anxiety

Skeletal Muscle Dysfunction

COPD & Obesity

CVD

Systemic Inflammation

Physical

OSA
To treat or not to treat?

Evidence from RCTs is needed to inform treatment guidelines.

*but*

Compelling pilot data indicates improved COPD outcomes with weight loss...*when coupled with resistance exercise training!*
knowledgements

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