ESFEN Congress Leipzig 2013

LLL Session - Nutritional support in respiratory diseases

New findings of meta-analysis in nutrition interventions for COPD and multimodal approaches

C. Pison (FR)
Nutritional Support in Respiratory Diseases – LLL 38

New findings of meta-analysis in nutrition interventions for COPD and multimodal approaches

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Grenoble, France

Leipzig, 4th of September 2014
Obstructive Lung Diseases

International Classification of Functioning ICF-2, WHO, 2001

Deficiency

Lungs
Oxidant stress, Hypoxia, Inflammation

Systemic
Oxidant stress, Hypoxia, Inflammation

FEV₁
SpO₂

BMI
Skeletal muscles

Activities

Dyspnea

6 MWD

Participation

Quality of life - Morbidity Mortality
Therapy at Each Stage of COPD

I: Mild
- FEV₁/FVC < 70%
- FEV₁ > 80% predicted

Add short-acting bronchodilator (when needed)

Active reduction of risk factor(s); influenza vaccination

II: Moderate
- FEV₁/FVC < 70%
- 50% ≤ FEV₁ < 80% predicted

Add regular treatment with one or more long-acting bronchodilators (when needed); Add rehabilitation

Add inhaled glucocorticosteroids if repeated exacerbations

III: Severe
- FEV₁/FVC < 70%
- 30% ≤ FEV₁ < 50% predicted

Add inhaled glucocorticosteroids if repeated exacerbations

IV: Very Severe
- FEV₁/FVC < 70%
- FEV₁ < 30% predicted or FEV₁ < 50% predicted plus chronic respiratory failure

Add long term oxygen if chronic respiratory failure. Consider surgical treatments
Nutritional needs in COPD

- Depending on their condition COPD patients can need up to 600 kcal /day more than healthy individuals

- “Nutritional supplementation should initially consist of adaptations in the patients’ dietary habits and should be extended to administration of energy-dense supplements”

Baarends et al. Am J Respir Crit Care Med 1997;155:549-54
Baarends et al. 1997;52:780-5
Schols et al. JPEN 1992;16: 364-8
Nici et al. AJRCCM 2006;173:1390-1413
Post prandial dyspnoea: fat vs. carbohydrate

- Acute effects of ONS, fat vs. carbohydrate, 11 subjects COPD, 62±8 yrs, FEV$_1$ 34±12% pred., BMI 22.6±2.3. Vermeeren et al. AJCN 2001;73:295-301

250 kcal fat rich oral supplement
250 kcal carbohydrate rich oral supplement

FIGURE 6. Difference between mean (±SEM) post- and preprandial shortness of breath score on a visual analogue scale (VAS) 30 and 60 min after consumption of a fat-rich (■) and a carbohydrate-rich (□) supplement. n = 11. ANOVA with postprandial value as the dependent variable, with treatment and period as fixed factors, and with patient as a random factor.
More not always better!

- Energy intake, 568 kcal/d vs. 800 kcal/d, 2 severe depleted groups of COPD, 19 vs. 20, 8-weeks in-pulmonary rehabilitation
  
**Nutritional intervention**

- Weekes et al. Thorax 2009;64:326-31
  + 194 kcal/d, + 11.8 g protein/d vs. Controls
  no changes in muscle strength and respiratory function
  St Georges + 10.1, MRC score + 1, ADL score + 1.5
Nutritional support in COPD treatment - Guidelines

- **2006 ERS /ATS guidelines. Nici et al. AJRCCM 2006;173:1390-1413**
  - BMI < 21
  - involuntary weight loss: >10% during last 6 months or >5% in the past month)
  - depletion in FFMI, <16 males, <15 females

- **2010 SPLF guidelines. RMR 2010;27:522-48**
  - No attempt to lose weight
  - Rehabilitation > nutritional supplementation in any cases, especially if under nutrition

- **2014 – ERS statement on Nutrition and COPD**
Nutritional support: essential during rehabilitation

- Risk of nutritional depletion in subjects, even normal weighted, undergoing Pulmonary Rehabilitation

  - **Steiner et al. Thorax 2003;58:745-51.**
  - **Goris et al. The British journal of nutrition 2003;89:725-31.**
  - **Slinde et al. Clinical nutrition 2003;22:159-65.**
  - **Creutzberg et al. Nutrition 2003;19:120-7**
  - **Weekes et al. Thorax 2010;64:326-31**
Nutritional intervention

Nutritional supplementation for stable chronic obstructive pulmonary disease (Review)

Ferreira IM, Brooks D, White J, Goldstein R

THE COCHRANE COLLABORATION®
Nutritional intervention changes body weight, kg

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Experimental Total</th>
<th>Control Total</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.7.1 Undernourished</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DeLetter 1991 (1)</td>
<td>1.2</td>
<td>0.4123</td>
<td>18</td>
<td>17</td>
<td>18.0%</td>
<td>1.20 [0.39, 2.01]</td>
</tr>
<tr>
<td>Ethimocou 1988 (2)</td>
<td>4.1</td>
<td>1.5071</td>
<td>7</td>
<td>7</td>
<td>1.3%</td>
<td>4.10 [1.15, 7.05]</td>
</tr>
<tr>
<td>Fuenzalida 1990 (3)</td>
<td>1.22</td>
<td>1.4284</td>
<td>5</td>
<td>4</td>
<td>1.5%</td>
<td>1.22 [-1.58, 4.02]</td>
</tr>
<tr>
<td>Lewis 1987 (4)</td>
<td>1.2</td>
<td>0.442</td>
<td>10</td>
<td>11</td>
<td>15.7%</td>
<td>1.20 [0.33, 2.07]</td>
</tr>
<tr>
<td>Otte 1989</td>
<td>1.36</td>
<td>0.4579</td>
<td>13</td>
<td>13</td>
<td>14.6%</td>
<td>1.36 [0.46, 2.26]</td>
</tr>
<tr>
<td>Rogers 1992</td>
<td>2.8</td>
<td>1.8243</td>
<td>15</td>
<td>12</td>
<td>0.9%</td>
<td>2.80 [-0.78, 6.38]</td>
</tr>
<tr>
<td>Schols 1995 (5)</td>
<td>2.4</td>
<td>0.5967</td>
<td>39</td>
<td>25</td>
<td>8.6%</td>
<td>2.40 [1.23, 3.57]</td>
</tr>
<tr>
<td>Sugawara 2010 (6)</td>
<td>1.91</td>
<td>0.7184</td>
<td>17</td>
<td>14</td>
<td>5.9%</td>
<td>1.91 [0.50, 3.32]</td>
</tr>
<tr>
<td>van Wetering 2010</td>
<td>2.8</td>
<td>0.9745</td>
<td>16</td>
<td>14</td>
<td>3.2%</td>
<td>2.80 [0.89, 4.71]</td>
</tr>
<tr>
<td>Weekes 2009</td>
<td>2.1</td>
<td>1.607</td>
<td>30</td>
<td>25</td>
<td>1.2%</td>
<td>2.10 [-1.05, 5.25]</td>
</tr>
<tr>
<td>Whittaker 1990</td>
<td>3</td>
<td>0.8944</td>
<td>6</td>
<td>4</td>
<td>3.8%</td>
<td>3.00 [1.25, 4.75]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>176</td>
<td>148</td>
<td>74.8%</td>
<td></td>
<td>1.73 [1.29, 2.17]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.06; Chi² = 11.21, df = 10 (P = 0.34); I² = 11%
Test for overall effect: Z = 7.70 (P < 0.00001)

1.7.2 Nourished

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Experimental Total</th>
<th>Control Total</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schols 1995</td>
<td>1.5</td>
<td>0.8061</td>
<td>33</td>
<td>38</td>
<td>4.7%</td>
<td>1.50 [-0.08, 3.08]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>33</td>
<td>38</td>
<td>4.7%</td>
<td></td>
<td>1.50 [-0.08, 3.08]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect: Z = 1.86 (P = 0.06)

1.7.3 Combined population of undernourished and nourished

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Experimental Total</th>
<th>Control Total</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowles 1988 (7)</td>
<td>2.05</td>
<td>3.1791</td>
<td>13</td>
<td>12</td>
<td>0.3%</td>
<td>2.05 [4.18, 8.28]</td>
</tr>
<tr>
<td>Steiner 2003</td>
<td>1.21</td>
<td>0.779</td>
<td>25</td>
<td>35</td>
<td>5.0%</td>
<td>1.21 [-0.32, 2.74]</td>
</tr>
<tr>
<td>Sugawara 2012</td>
<td>1.5</td>
<td>0.4486</td>
<td>17</td>
<td>14</td>
<td>15.2%</td>
<td>1.50 [0.62, 2.38]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>55</td>
<td>61</td>
<td>20.5%</td>
<td></td>
<td>1.44 [0.68, 2.19]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.14, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 3.72 (P = 0.00002)

Total (95% CI)

<table>
<thead>
<tr>
<th>Mean Difference</th>
<th>SE</th>
<th>Experimental Total</th>
<th>Control Total</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>264</td>
<td>247</td>
<td>100.0%</td>
<td></td>
<td>1.62 [1.27, 1.96]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 11.66, df = 14 (P = 0.63); I² = 0%
Test for overall effect: Z = 9.24 (P < 0.000001)
Test for subgroup differences: Chi² = 0.45, df = 2 (P = 0.80); I² = 0%

17 studies, 8 combined with exercise, increased body weight
Nutritional intervention changes fat-free mass, kg

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Supplement Total</th>
<th>Control Total</th>
<th>Std. Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.8.1 Undernourished</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sugawara 2010 (1)</td>
<td>0.8329 0.3713</td>
<td>17 15</td>
<td>0.83 [0.11, 1.56]</td>
</tr>
<tr>
<td>Schols 1995 (2)</td>
<td>1.0495 0.2735</td>
<td>39 25</td>
<td>1.05 [0.51, 1.59]</td>
</tr>
<tr>
<td>van Wetering 2010 (3)</td>
<td>1.5066 0.4282</td>
<td>15 14</td>
<td>1.51 [0.67, 2.35]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>71 54</td>
<td></td>
<td>1.08 [0.70, 1.47]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 1.45, df = 2 (P = 0.48); I² = 0%
Test for overall effect: Z = 5.54 (P < 0.00001)

| **1.8.2 Adequately nourished** |                 |               |                                       |
| Schols 1995                    | 0.2651 0.239    | 33 38         | 0.27 [-0.20, 0.73]                    |
| **Subtotal (95% CI)**          | 33 38         |               | 0.27 [-0.20, 0.73]                    |

Heterogeneity: Not applicable
Test for overall effect: Z = 1.11 (P = 0.27)

| **1.8.3 Combined population of undernourished and nourished patients** |                 |               |                                       |
| Steiner 2003                  | -0.3712 0.2642  | 25 35         | -0.37 [-0.89, 0.15]                   |
| Sugawara 2012 (4)             | 0.3532 0.3641   | 17 14         | 0.35 [-0.36, 1.07]                    |
| **Subtotal (95% CI)**         | 42 49         |               | -0.05 [-0.76, 0.65]                   |

Heterogeneity: Tau² = 0.16; Chi² = 2.59, df = 1 (P = 0.11); I² = 61%
Test for overall effect: Z = 0.15 (P = 0.88)

**Total (95% CI)**

146 141 100.0% 0.57 [0.04, 1.09]

Heterogeneity: Tau² = 0.33; Chi² = 22.28, df = 5 (P = 0.0005); I² = 78%
Test for overall effect: Z = 2.11 (P = 0.03)
Nutritional intervention changes in 6-MWD, m

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental N</th>
<th>Control N</th>
<th>Mean Difference (SE)</th>
<th>I^2 (%)</th>
<th>Weight</th>
<th>Difference (95% CI)</th>
<th>Subtotal (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 6-minute walk test</td>
<td>DeLette 1991 (1)</td>
<td>18</td>
<td>17</td>
<td>36.58 (8.7393)</td>
<td>33.1 %</td>
<td>36.58 [ 19.45, 53.71 ]</td>
<td><strong>100.0 %</strong> 39.96 [ 22.66, 57.26 ]</td>
</tr>
<tr>
<td>2 12-minute walk test</td>
<td>Ethimiou 1988 (2)</td>
<td>7</td>
<td>7</td>
<td>47 (23.3421)</td>
<td>11.1 %</td>
<td>47.00 [ 1.25, 92.75 ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sugawara 2010 (3)</td>
<td>17</td>
<td>13</td>
<td>54.12 (15.1764)</td>
<td>20.0 %</td>
<td>54.12 [ 24.37, 83.87 ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sugawara 2012 (4)</td>
<td>17</td>
<td>14</td>
<td>105 (37.5965)</td>
<td>5.0 %</td>
<td>105.00 [ 31.31, 178.69 ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>van Wetering 2010 (5)</td>
<td>16</td>
<td>14</td>
<td>21.5 (9.6125)</td>
<td>30.9 %</td>
<td>21.50 [ 2.66, 40.34 ]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>100.0 %</strong> -0.04 [-255.61, 255.53 ]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 159.25; Chi^2 = 7.30, df = 4 (P = 0.12); I^2 = 45%</td>
<td>Test for overall effect: Z = 4.53 (P &lt; 0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Incremental shuttle walk test</td>
<td>Otte 1989</td>
<td>13</td>
<td>15</td>
<td>-130.3 (79.9521)</td>
<td>50.1 %</td>
<td>-130.30 [-287.00, 26.40 ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rogers 1992</td>
<td>15</td>
<td>12</td>
<td>130.49 (80.3839)</td>
<td>49.9 %</td>
<td>130.49 [-27.06, 288.04 ]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>100.0 %</strong> 17.40 [-126.41, 161.21 ]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: not applicable</td>
<td>Test for overall effect: Z = 0.24 (P = 0.81)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi^2 = 0.19, df = 2 (P = 0.91), I^2 = 0.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Nutritional intervention alone is not enough

**CHRONIC ILLNESS**
- e.g. Chronic heart failure,
- Chronic obstructive pulmonary disease,
- Chronic kidney disease,
- Chronic infection & Sepsis,
- Cancer

**ORGAN FAILURE**
**SPECIFIC DISTURBANCES**
- Hypoxia,
- Acidosis,
- Oxidative stress,
- Growth factor impairments …

**Anorexia**

**Inflammation**

**Insulin resistance**

**Hypogonadism**

**Anemia**

**FAT LOSS**

**MUSCLE WASTING**

- Weight loss
- Weakness & Fatigue: reduced muscle strength, VO₂ max, and physical activity

Multimodal Intervention

Schols et al. AJRCCM 1995;152;1268-74

• Patients 233, FEV₁ 35 ± 5 %
• Duration 8 weeks, in-patient rehabilitation

• Intervention - exercise + education
  - exercise + education + nutrition + placebo
  - exercise + education + nutrition + anabolic steroids

  Exercise training: - endurance
  - low impact conditioning exercises
  - no strength training

• Results
  • Increase in body weight with nutrition alone & anabolic steroids
  • Enhanced increase in FFM / Pi-max with anabolic steroids
Multimodal Intervention

Schols et al. AJRCCM 1998;157;1791-7

### Multivariate Analysis of Predictors of Mortality: Prospective Study

<table>
<thead>
<tr>
<th>Variables</th>
<th>RR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in weight</td>
<td>0.996</td>
<td>0.992–0.999</td>
<td>0.01</td>
</tr>
<tr>
<td>Change in P(_{\text{max}})</td>
<td>0.990</td>
<td>0.976–1.004</td>
<td>NS</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P versus A</td>
<td>0.753</td>
<td>0.447–1.267</td>
<td>NS</td>
</tr>
<tr>
<td>N versus A</td>
<td>0.872</td>
<td>0.530–1.432</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>0.868</td>
<td>0.803–0.939</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>FEV(_1)</td>
<td>0.983</td>
<td>0.962–1.003</td>
<td>NS</td>
</tr>
<tr>
<td>IVC</td>
<td>0.995</td>
<td>0.982–1.008</td>
<td>NS</td>
</tr>
<tr>
<td>Pa(_o_2)</td>
<td>0.877</td>
<td>0.751–1.024</td>
<td>NS</td>
</tr>
<tr>
<td>Pa(_c_0_2)</td>
<td>0.977</td>
<td>0.707–1.352</td>
<td>NS</td>
</tr>
<tr>
<td>Age, yr</td>
<td>1.056</td>
<td>1.022–1.090</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Definition of abbreviation: P\(_{\text{max}}\) = maximal static inspiratory pressure. For other definitions, see Tables 1 and 2.*

* Entered as time-dependent covariate.*

![Graph showing weight gain](image)
• **Patients** 102, 66±9 yrs, FEV\(_1\) 58±17 %, BMI 26.1±4.4
  97, 67±9 yrs, FEV\(_1\) 60±15 %, BMI 27.3±4.7
  Wmax < 70%, 20% depleted

• **Duration** 2 years

• **Intervention** 4 months home multimodal intervention,
  20 maintenance care
  *versus* usual care

• **Results**
  • 4 months: better FFM, QoL, Wmax, endurance, MRC
dyspnea score, hand grip, 6MWD
  • 2 years : better QoL, MRC score, endurance, 6MWD
Multimodal Intervention


[Graph showing changes in 6MWD (meters) from baseline over time (in months) for INTERCOM muscle wasted, INTERCOM muscle non-wasted, Usual Care muscle non-wasted, and Usual Care muscle muscle wasted.]
Multimodal Intervention

testosterone

Casaburi et al. Am J Crit Care Med 2004;170;870-8

47 male patients with COPD, mean $FEV_1 = 40\%$
randomized, double blind, controlled
4 groups, resistance exercise, 100 mg
testosterone IM/week, 10 weeks
Multimodal Intervention

**PUFA**


80 COPD, 8 weeks rehabilitation plus oral nutritional supplement (Respifor®)

Double blind, controlled design: oral n-3 PUFA, 9 g/day during 8 weeks
Multimodal Intervention

IRAD2 study in Chronic Respiratory Failure

- **Patients**  
  60, 66.6±9.6 yrs, BMI 21.5±3.8  
  62, 65.1±9.6 yrs, BMI 21.4±4.0

- **Duration**  
  12 weeks, 12 months follow-up

- **Intervention**  
  - Education + Exercise + ONS + oral Testosterone  
  - Education

- **Results**  
  - 3 months: increases in body weight, FFM,QF, Hb, endurance, Wmax, QoL in women  
  - 15 months : better survival per-protocol analysis
Multimodal Intervention

IRAD2 study in Chronic Respiratory Failure

Control group

D\textsubscript{1}: first day of education (Home)

D\textsubscript{90}=M\textsubscript{3}: last investigations (Hospital)

D\textsubscript{270}=M\textsubscript{9}

D\textsubscript{450}=M\textsubscript{15}

D\textsubscript{inclusion}: first investigations

D\textsubscript{random}.

D\textsubscript{1}: first day of rehabilitation (Home)

D\textsubscript{90}=M\textsubscript{3}: last investigations (Hospital)

Rehabilitation group
Multimodal Intervention

IRAD2 study in Chronic Respiratory Failure
Multimodal Intervention

IRAD2 study in Chronic Respiratory Failure

![Graph showing survival analysis and number at risk for different groups.](image-url)
Multimodal Intervention

IRAD2 study in Chronic Respiratory Failure

*Pison et al. Thorax 2011;66:953-60*
Multimodal Intervention
NIV

Budweiser et al. Respir Care 2006;51:126-32
### TABLE 1: Body composition in lung volume reduction surgery (LVRS) and respiratory rehabilitation (RR) groups

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Fat-free mass</th>
<th></th>
<th></th>
<th>Fat mass</th>
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<tbody>
<tr>
<td></td>
<td>Baseline g</td>
<td>12 month</td>
<td>36 month</td>
<td>60 month</td>
<td>Baseline g</td>
<td>12 month</td>
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<tr>
<td>Upper limbs</td>
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<tr>
<td>LVRS</td>
<td>5800 ± 270</td>
<td>+4.1*</td>
<td>+3.8</td>
<td>+3.5</td>
<td>2560 ± 145</td>
<td>+4.6*</td>
</tr>
<tr>
<td>RR</td>
<td>5731 ± 284</td>
<td>+0.7</td>
<td>-2.2</td>
<td>-2.3</td>
<td>2572 ± 138</td>
<td>-2.1</td>
</tr>
<tr>
<td>p-value</td>
<td>0.76</td>
<td>0.04</td>
<td>0.01</td>
<td>0.01</td>
<td>0.95</td>
<td>0.02</td>
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<td>Trunk</td>
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</tr>
<tr>
<td>LVRS</td>
<td>26256 ± 2310</td>
<td>+3.7</td>
<td>+3.5</td>
<td>+3.2</td>
<td>8470 ± 1230</td>
<td>+9.7**</td>
</tr>
<tr>
<td>RR</td>
<td>26123 ± 1957</td>
<td>+0.2</td>
<td>-4.6</td>
<td>-4.7</td>
<td>8485 ± 1245</td>
<td>-1.3</td>
</tr>
<tr>
<td>p-value</td>
<td>0.91</td>
<td>0.05</td>
<td>0.02</td>
<td>0.02</td>
<td>0.91</td>
<td>0.007</td>
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<tr>
<td>Lower limbs</td>
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<tr>
<td>LVRS</td>
<td>15620 ± 1540</td>
<td>+7.4**</td>
<td>+7.1**</td>
<td>+5.1*</td>
<td>6630 ± 346</td>
<td>+3.9</td>
</tr>
<tr>
<td>RR</td>
<td>15590 ± 1348</td>
<td>+1.4</td>
<td>-2.3</td>
<td>-2.5</td>
<td>6644 ± 233</td>
<td>-2.3</td>
</tr>
<tr>
<td>p-value</td>
<td>0.89</td>
<td>0.03</td>
<td>0.005</td>
<td>0.007</td>
<td>0.89</td>
<td>0.01</td>
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<tr>
<td>Total body</td>
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</tr>
<tr>
<td>LVRS</td>
<td>47300 ± 3657</td>
<td>+6.0**</td>
<td>+5.3**</td>
<td>+4.0*</td>
<td>18810 ± 1024</td>
<td>+7.1**</td>
</tr>
<tr>
<td>RR</td>
<td>47120 ± 3216</td>
<td>+1.2</td>
<td>-4.6*</td>
<td>-4.7*</td>
<td>18842 ± 1176</td>
<td>-1.9</td>
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<td>0.03</td>
<td>0.006</td>
<td>0.01</td>
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</tr>
</tbody>
</table>

Data are presented as mean ± sd or % change from baseline. **: p < 0.01; *: p ≤ 0.05.
Multimodal Intervention

lung transplantation

All indications, n = 204
Multimodal Intervention

- Low energy intake
- Inactivity
- Hypogonadism
- Inflammation
- Insulin-resistance
- Others, hypoxia, ..

Multimodal approach of undernutrition

Integrated care
- Counseling
- ONS
- Exercise
- Androgens
- others:
  - n-3 FA
  - N-acetylcysteine
  - anti-TNF
  - etc.
Personalized & Comprehensive Cares

- Patient perspectives and objectives
- Smoking
- Infection
- Respiratory mechanical disadvantages: long-acting bronchodilators
- Hypoxemia
- Energy intake deficit
- Promotion of Daily Physical Activities
- Modulation of systemic inflammation, \textit{omega-3}
- \textit{Lung volume reduction}
- \textit{Lung transplantation}
Conclusions

- Multimodal Evaluation
- Multimodal Intervention
- Interventions at early and advanced disease, to be tailored to the patient perspective
- Role of home disease management