INTENSIVE PULMONARY REHABILITATION FOR LUNG CANCER PATIENTS: IS IT FEASIBLE? IS IT EFFECTIVE?

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Vienna, Austria
Background and Introduction

- Surgical resection remains the best curative option for patients with early-stage I-II NSCLC and in selected patients with locally advanced (IIIA) disease.

- Approximately 20 – 25% of patients have anatomically resectable NSCLC at the time of cancer diagnosis, however poor performance status due to comorbidities, such as COPD/emphysema limit surgical eligibility.

- Pulmonary rehabilitation (PR) has been definitively proven to increase performance status, with most studies showing improvements after 4 - 6 weeks of training.

- 4 – 6 week treatment delay imposed by preoperative PR has limited PR as a preoperative strategy to improve surgical eligibility in the cancer setting where significant delays in definitive cancer therapies imposed by a course of PR is a major concern.

References:

Benzo R et al. Lung Cancer 2011
McCarthy B et al. Cochrane Database Syst Rev. 2015
Powels S et al. Resp Med 2015
INTENSIVE PULMONARY REHABILITATION FOR NONSMALL CELL LUNG CANCER (NSCLC) PATIENTS: IS IT FEASIBLE? IS IT EFFECTIVE?

Abstract: PS065

• Objective:
  – Determine the minimal duration of PR that confers significant improvements in performance status, using VO$_2$\text{max} and 6MWD as markers of performance status
# INTENSIVE PULMONARY REHABILITATION FOR NONSMALL CELL LUNG CANCER (NSCLC) PATIENTS: IS IT FEASIBLE? IS IT EFFECTIVE?

**Abstract:**

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<tr>
<th><strong>Inclusion Criteria</strong></th>
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<tbody>
<tr>
<td>Adults (male, female), age &gt;18</td>
<td>Unstable pulmonary, cardiovascular, musculoskeletal, psychiatric or liver disease</td>
</tr>
<tr>
<td>Diagnosis of NSCLC, stage I-IIIB</td>
<td>Respiratory failure (room air SaO2 &lt; 88% at rest)</td>
</tr>
<tr>
<td>Concomitant diagnosis of COPD, GOLD stages III-IV</td>
<td>Unwillingness/unable to cooperate with the PR program</td>
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</tbody>
</table>
Study Design

Prospective study
Anatomically resectable NSCLC, Stage I-II, Gold Stage III-IV COPD
Surgical resection denied due to poor performance status
(VO2 max (12 – 14.9 ml/kg/min); *6MWD < 200m

Assessment of functional parameters:
(*CPET, Borg scales, *6MWT, *PFTs)

*PR: High intensity training
Aerobic/resistance training 3 days/week
Repeat functional testing after week # 2

Continue PR
Repeat functional testing after week 3
(except PFTs)

Repeat all functional parameters

All bronchodilators continued as previously prescribed. Exercise work load set at 60-70% of VO₂max reached during CPET

3 minute warm up/cool down
High intensity training: Work load intensity and/or duration increased to 70-80% VO₂ and/or 20 minutes

Work load intensity and/or duration increased to 80% VO₂ and/or 30minutes

PR weeks #4-12:
work load intensity maintained at 80% VO₂

*6MWT = 6-minute walk test; 6MWD = 6-minute walk distance; CPET = cardiopulmonary exercise testing; VO₂ = oxygen consumption; PR = pulmonary rehabilitation; PFTs = pulmonary function tests
Primary outcome measures

- Change from baseline after 2, 3, and 12 weeks of PR:
  - VO₂max (mL/kg/min)
  - 6MWD
  - Borg scores

Secondary outcome measures

- Change from baseline after 2, 3, and 12 weeks of PR:
  - PFTs: (FEV1, FEV1/FVC, DLCO)

Safety issues

- Cardiovascular: hypertension/hypotension, arrhythmias, syncope/near-syncope, chest pain
- Pulmonary: acute respiratory distress or desaturation requiring medical intervention/interruption of PR
- Musculoskeletal: bone/joint pain or swelling requiring treatment interruption

Statistical Analysis

- Descriptive information collected
- Comparison of changes in VO₂max from baseline: a repeated measures analysis of variance (RM-ANOVA)
- Significance of results prespecified for p<0.05
## Characteristics of Participants

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients, N = 92</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean)</td>
<td>63 ± 8</td>
</tr>
<tr>
<td>Gender (n, %)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>68 (74)</td>
</tr>
<tr>
<td>BMI, kg/m² (mean)</td>
<td>27.13 ± 4.38</td>
</tr>
<tr>
<td>Cancer histology (n, %)</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>57 (62)</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>34 (37)</td>
</tr>
<tr>
<td>Adenosquamous</td>
<td>1</td>
</tr>
<tr>
<td>COPD Gold Stage (n, %)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>89 (97)</td>
</tr>
<tr>
<td>IV</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Mean # comorbidities (excluding cancer, COPD)</td>
<td>2(2)</td>
</tr>
<tr>
<td>Tobacco use history</td>
<td></td>
</tr>
<tr>
<td>Prior tobacco use</td>
<td>84 (91)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>8 (9)</td>
</tr>
<tr>
<td>Functional parameters</td>
<td>PR Interval</td>
</tr>
<tr>
<td>-----------------------</td>
<td>-------------</td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Borg Score</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>8</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7</td>
</tr>
<tr>
<td>6MWT</td>
<td></td>
</tr>
<tr>
<td>Distance, meters</td>
<td>68</td>
</tr>
<tr>
<td>PFTs</td>
<td></td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>1.26</td>
</tr>
<tr>
<td>FEV₁ (% pred.)</td>
<td>44 ± 9</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>2.10 ± 3</td>
</tr>
<tr>
<td>FVC (% pred.)</td>
<td>68 ± 3</td>
</tr>
<tr>
<td>FEV₁/FVC (% pred.)</td>
<td>65 ± 2</td>
</tr>
<tr>
<td>DLCO (%pred)</td>
<td>66 ± 4</td>
</tr>
<tr>
<td>CPET</td>
<td></td>
</tr>
<tr>
<td>VO₂ max (ml/kg/min)</td>
<td>12.2 ± 1.6</td>
</tr>
<tr>
<td>VO₂ max (L)</td>
<td>1.15 ± 0.6</td>
</tr>
<tr>
<td>VO₂/AT (ml/kg/min)</td>
<td>12.1 ± 1.1</td>
</tr>
<tr>
<td>VO₂/AT (L)</td>
<td>0.95 ± 0.7</td>
</tr>
<tr>
<td>Work load (W)</td>
<td>67 ± 4</td>
</tr>
<tr>
<td>O₂ pulse (ml/bpm)</td>
<td>8.1 ± 1.7</td>
</tr>
<tr>
<td>VE/max (L)</td>
<td>36 ± 9</td>
</tr>
<tr>
<td>VE/VCO₂</td>
<td>35 ± 9</td>
</tr>
<tr>
<td>BR (%)</td>
<td>17 ± 8</td>
</tr>
</tbody>
</table>

CPET: cardiopulmonary exercise tests; B: baseline; wks = weeks; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; TLC: total lung capacity; DLCO: diffusion lung capacity of CO; VO₂: oxygen uptake; VO₂@AT: oxygen uptake at anaerobic threshold; VE: minute ventilation; Oxygen pulse: oxygen uptake/heart rate; BR: Breathing reserve; VE/VCO₂: ventilatory equivalent for CO₂.
Changes in functional performance from baseline to post 12 weeks:

- **Dyspnea** and **Fatigue** levels over time.

- **Changes in Borg Scale Over Time**:
  - **Baseline**: 8
  - **Week 2**: 7
  - **Week 3**: 6
  - **Post 12 weeks**: 5

- **Distance, meters** and **VO2 max (ml/kg/min)**
- **Work load (W)**

- **P < 0.05**
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Abstract:

• Conclusions:

  – A program of high intensity PR appears to be an effective and feasible intervention which is well tolerated among lung cancer patients with concomitant moderate to severe COPD.

  – Significant improvements in performance status, as measured by changes in VO2max and 6MWD may be seen as early as 2 weeks after initiation of an intensive PR program.

  – These findings have significant clinical implications and may improve treatment options among NSCLC patients considered inoperable due to poor baseline performance status.
Thank you.............

Any Questions?
Changes in Borg Scale Over Time

<table>
<thead>
<tr>
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<th>Baseline</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Post 12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>8</td>
<td>7</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7</td>
<td>6</td>
<td>5</td>
<td>5</td>
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Axis Title
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**PR program adherence:**  
- At 2 and 3 weeks: 100%  
- After 12 weeks: 76/92 (83%)  
  - Reasons for nonadherence:  
    - Returned home after definitive cancer therapy (n=11)  
    - Lost to follow up (n=5)  

**Exercise-related adverse events:**  
- Transient hypotension with >20 mmHg decline in systolic blood pressure, which normalized after discontinuing exercise (n=1)
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Outcomes

- Primary outcome measures:
  - Change from baseline in VO2peak (mL/kg/min) after 2, 3, and 12 weeks of PR
  - Change from baseline in 6MWD after 2, 3, and 12 weeks of PR
- Secondary outcome measures
  - Change in Borg scores and PFTs (FEV1, FEV1/FVC, DLCO) from baseline
- Safety issues
  - Cardiovascular: hyper-/hypotension, arrhythmias, syncope/near-syncope, chest pain
  - Pulmonary: desaturation requiring medical intervention; acute respiratory distress requiring medical intervention/interruption of PR
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• Muscle groups targeted/training exercises:
  – Endurance training:
    • Treadmill, upper and lower extremity cycle ergometry
  – Resistance training:
    • Chest and upper extremity muscle groups: chest press, vertical traction and lateral pulls
    • Lower extremity muscle groups: leg press/curl, hip abductors/adductors and leg extension
    • Patients were asked to perform 3 sets of 15 repetitions at 60% of the 1 repetition maximum.
  • Exercise training was conducted under one-on-one supervision of MDACC staff physical and occupational therapists.