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

2018
28-30 JUNE
VIENNA, AUSTRIA
SUPPORTIVE CARE MAKES EXCELLENT CANCER CARE POSSIBLE


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**MASCC 2018**

**Vienna, Austria**

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center


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**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.


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Abstract: PS065

- Objective:
  - Determine the minimal duration of PR that confers significant improvements in performance status, using $VO_2$max and 6MWD as markers of performance status

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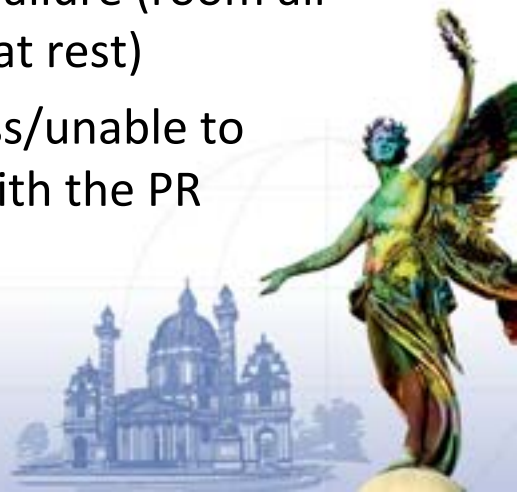
## *Inclusion Criteria*

- Adults (male, female), age >18
- Diagnosis of NSCLC, stage I-IIB
- Concomitant diagnosis of COPD, GOLD stages III-IV

## *Exclusion Criteria*

- Unstable pulmonary, cardiovascular, musculoskeletal, psychiatric or liver disease
- Respiratory failure (room air SaO2 < 88% at rest)
- Unwillingness/unable to cooperate with the PR program



# 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)**

All bronchodilators continued as previously prescribed. Exercise work load set at 60-70% of $VO_2$max reached during CPET

↓

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

3 minute warm up/cool down
High intensity training: Work load intensity and/or duration increased to 70-80% $VO_2$ and/or 20 minutes

↓

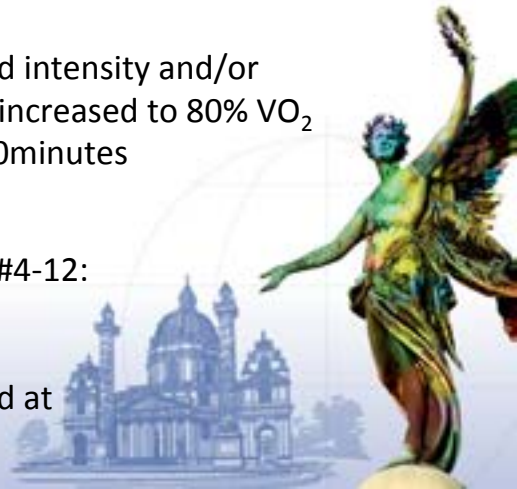
**Continue PR**
**Repeat functional testing after week 3**
**(except PFTs)**

Work load intensity and/or duration increased to 80% $VO_2$ and/or 30minutes

↓

**Repeat all functional parameters**

PR weeks #4-12: work load intensity maintained at 80% $VO_2$



*6MWT = 6-minute walk test; 6MWD = 6-minute walk distance; CPET = cardiopulmonary exercise testing; $VO_2$ = oxygen consumption; PR = pulmonary rehabilitation; PFTs = pulmonary function tests

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## *Primary outcome measures*

- ***Change from baseline after 2, 3, and 12 weeks of PR:***
  - $VO_2$max (mL/kg/min)
  - 6MWD
  - Borg scores

**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 $p<0.05$**

## *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

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# Characteristics of Participants

| Parameter | All Patients, N = 92 |
|---|---|
| Age, years (mean) | 63 ± 8 |
| Gender (n, %) | |
| Male | 68 (74) |
| BMI, kg/m$^2$ (mean) | 27.13 ± 4.38 |
| Cancer histology (n, %) | |
| Adenocarcinoma | 57 (62) |
| Squamous cell carcinoma | 34 (37) |
| Adenosquamous | 1 |
| COPD Gold Stage (n, %) | |
| III | 89 (97) |
| IV | 3 (3) |
| Mean # comorbidities (excluding cancer, COPD) | 2(2) |
| Tobacco use history | |
| Prior tobacco use | 84 (91) |
| Current smoker | 8 (9) |

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# Pulmonary Function and CPET results post PR

| | | PR Interval | | | | | |
|---|---|---|---|---|---|---|---|
| Functional parameters | Baseline | Wk 2 | P-value: B to 2 wks | Week 3 | P-value: B to 3 wks | Post 12 wks | P-value: B- to 12 wks |
| **Borg Score** | | | | | | | |
| Dyspnea | 8 | 7 | NS | 7 | NS | 7 | NS |
| Fatigue | 7 | 6 | NS | 5 | NS | 6 | NS |
| **6MWT** | | | | | | | |
| Distance, meters | 68 | 144 | 0.002 | 158 | 0.002 | 136 | 0.003 |
| **PFTs** | | | | | | | |
| $FEV_1$ (L) | 1.26 | 1.64 | NS | 1.67 | NS | 1.55 | NS |
| $FEV_1$ (% pred.) | 44 ± 9 | 49 ± 8 | NS | 52 ± 4 | NS | 51 ± 5 | NS |
| FVC (L) | 2.10 ± 3 | 2.26 ± 7 | NS | 2.33 ± 4 | NS | 2.28 ± 2 | NS |
| FVC (% pred.) | 68 ± 3 | 71 ± 5 | NS | 72 ± 3 | NS | 70 ± 1 | NS |
| $FEV_1$/FVC (% pred.) | 65 ± 2 | 74 ± 6 | NS | 75 ± 7 | NS | 72 ± 4 | NS |
| DLCO (%pred) | 66 + 4 | 70 + 2 | NS | 71 + 2 | NS | 69 + 5 | NS |
| **CPET** | | | | | | | |
| $VO_2$ max (ml/kg/min) | 12.2 ± 1.6 | 19.3 ± 2.1 | <.001 | 19.7 ± 2.1 | <.001 | 17.3 ± 2.7 | <.001 |
| $VO_2$ max (L) | 1.15 ± 0.6 | 1.65 ± 0.3 | <.002 | 1.73 ± 0.2 | <.001 | 1.53 ± 0.2 | 0.017 |
| $VO_2$/AT (ml/kg/min) | 12.1 ± 1.1 | 15.8 ± 1.4 | 0.016 | 16.1 ± 1.5 | 0.019 | 15.1 ± 1.3 | 0.016 |
| $VO_2$/AT (L) | 0.95 ± 0.7 | 1.31 ± 0.4 | 0.006 | 1.37 ± 0.2 | 0.006 | 1.24 ± 0.3 | 0.012 |
| Work load (W) | 67 ± 4 | 84 ± 6 | 0.001 | 87 ± 5 | 0.001 | 77 ± 3 | 0.003 |
| O2 pulse (ml/bpm) | 8.1 ± 1.7 | 12.4 ± 3.5 | 0.006 | 12.9 ± 4.6 | 0.006 | 11.7 ± 2.1 | 0.007 |
| VE/max (L) | 36 ± 9 | 47 ± 6 | NS | 51 ± 3 | NS | 45 ± 4 | NS |
| VE/VCO2 | 35 ± 9 | 28 ± 5 | 0.002 | 26 ± 4 | 0.002 | 30 ± 3 | 0.017 |
| BR (%) | 17 ± 8 | 16 ± 7 | NS | 14 ± 6 | NS | 15 ± 6 | NS |

CPET: cardiopulmonary exercise tests; B: baseline; wks = weeks; $FEV_1$: 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; $VE/VCO_2$: ventilatory equivalent for $CO_2$

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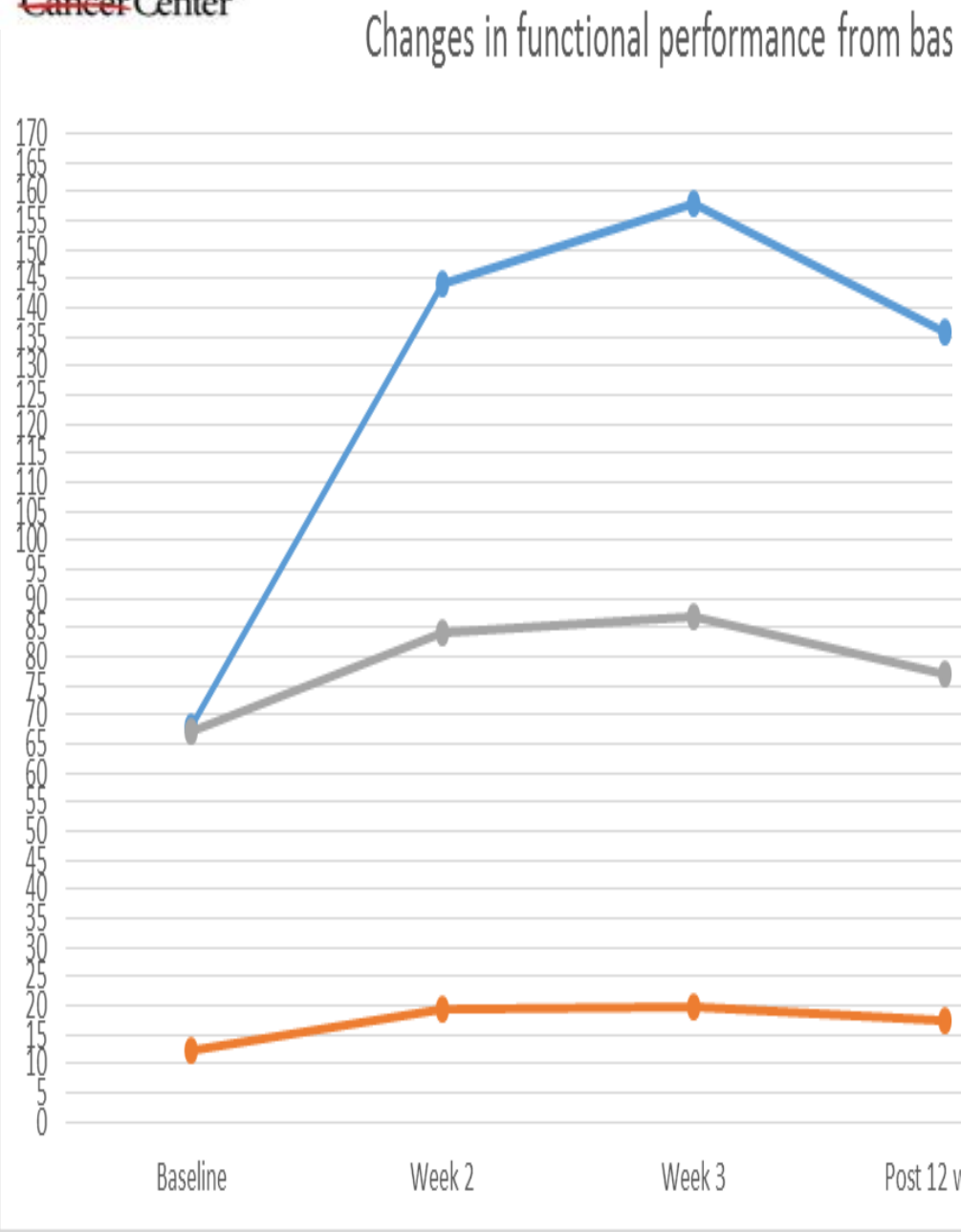


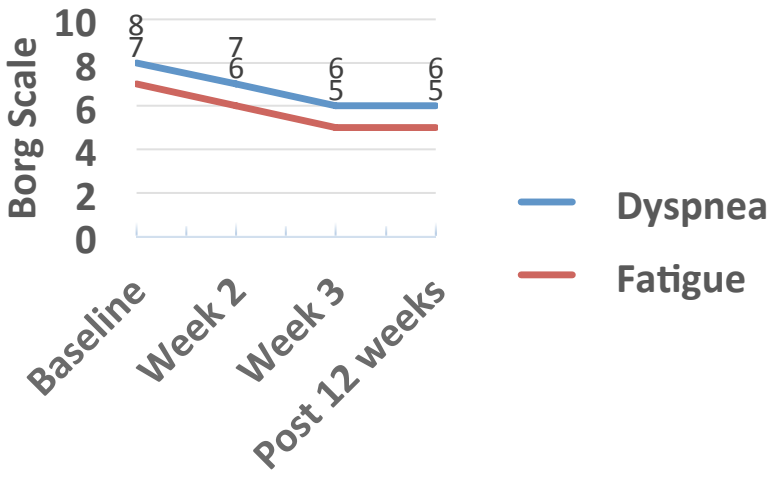


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- ***Conclusions:***
  - A program of high intensity PR appears to be an effective and feasible intervention which is well tolerated among lung cancer patients with concomitant moderate to severe COPD.
  - Significant improvements in performance status, 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.

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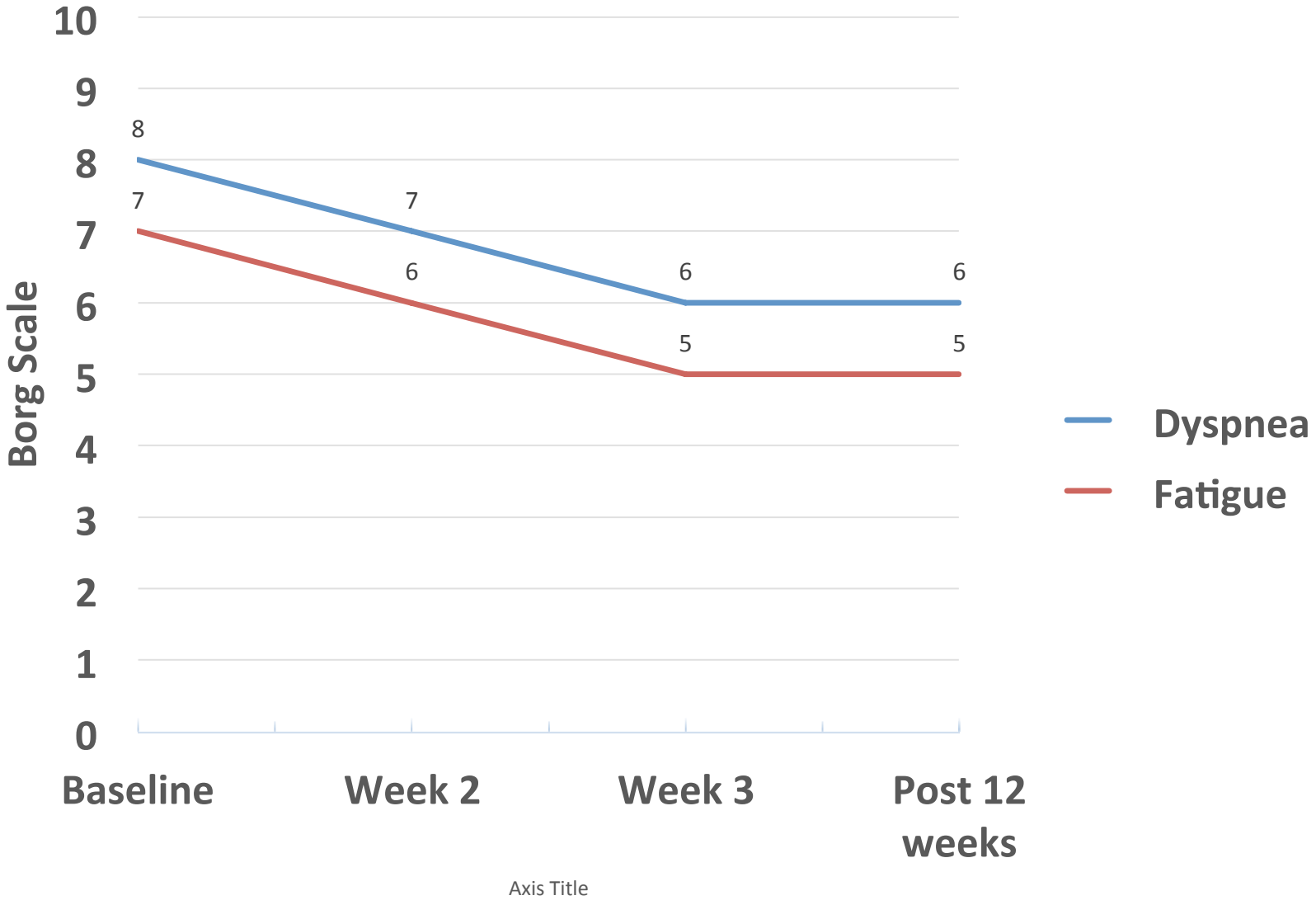
# Thank you……..

## Any Questions?

# Changes in Borg Scale Over Time

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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
      - Musculoskeletal: bone/joint pain/swelling requiring interruption of therapy

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- Exclusion criteria
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  - Respiratory failure (SaO2 < 885 on room air at rest)
  - Unwillingness to cooperate with the PR program

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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.