The role of respiratory muscle dysfunction in exercise limitation and dyspnea: Rationale for IMT
Content

- Contribution of load/capacity imbalance of respiratory muscles to dyspnea and exercise limitation

- Interaction between work of breathing and peripheral muscle fatigue during exercise
Factors related to exercise limitation

- Lungs and Airways
- Respiratory Muscles
- Heart and Circulation
- Peripheral Muscles
- Fear
- Anxiety
- Motivation
Intensity ⊗ Quality

Measure: Modified Borg

BREATHLESSNESS

Measure: EMGdi/EMGdi,max

Cortex

Neural Respiratory Drive

Healthy (exercise)
Lung disease
Obesity
Heart failure
Other conditions (e.g., anemia, hypoxia, altitude, aging)

Respiratory muscle weakness

Capacity of Respiratory Muscles ⊗ Respiratory Muscles ⊗ Load on Respiratory Muscles
Table 3. Muscular Sensations

1. **Effort**: the intensity of the voluntary motor command; mediated by cerebral cortex
2. **Tension**: the tension developed by muscle; transduced by tendon organs via afferents
3. **Displacement**: the extent and velocity of muscle contraction; mediated by muscle spindle and joint receptors via afferents
4. **Fatigue/Pain**: ischemia, overuse; stimulate small free nerve endings in muscle
5. **Appropriateness**: intensities of above sensations are learned through behavioral mechanisms

Respiratory Muscles

Lung

Mechano-receptors

Chemo-receptors

Ventilation

Motor Cortex

Dyspnea (Affective Unpleasantness)

Limbic System Activation

Dyspnea (Sensory Intensity)

Somatosensory Cortex

Brainstem Respiratory Control Center

Respiratory Neural Drive

Neuromechanical Dissociation

Respiratory Muscles

Lung

Mechano-receptors

Proprio-receptors

Chemoreceptors
Load on Respiratory Muscles

Ventilation
Elastic Resistance (Cw+Lung)
Airway Resistance

Capacity of the Respiratory Muscles

Substrate / O2
Force (pressure generating capacity)
Endurance
LOAD
RESPIRATORY MUSCLES

- VENTILATION (BOTH EL + RES)
- DYN HYPERINFLATION (ELASTIC)
- AIRWAY RESISTANCE (RESISTIVE)
- EDEMA - FIBROSIS (ELASTIC)
- CHEST WALL (ELASTIC)
- $T_i/T_{tot}$
CAPACITY RESPIRATORY MUSCLES

- EMPHYSEMA
- CHRONIC HEART FAILURE
- INACTIVITY
- HYPERCAPNIA - HYPOXAEANIA
- CATABOLISM
- DRUGS (CORTICOSTEROIDS)
- INFLAMMATION
- MALNUTRITION
- ELECTROLYTE DISTURBANCES
Respiratory Muscle Weakness in COPD

$P_{max} \%\text{ pred}$

Normals

COPD
Dysfunction or Adaptation?

Load vs. Capacity of Respiratory Muscles during Exercise

From: Update in the Understanding of Respiratory Limitations to Exercise Performance in Fit, Active Adults
Expiratory flow limitation

Volume

Flow

IC

VT expansion limited
BF
Rest and Exercise

Adapted from O’Donnell DE. AJRCCM 2006;3:180-184
Length-Tension Relationship

Figure 7. Length-tension curve of the diaphragm. When a muscle is activated at lengths longer than optimal (Lo) or less than optimal, force output decreases. Lung volume is used as an index of muscle length and pressure as an index of tension.
Velocity-Tension Relationship

Figure 8. Velocity-tension relationship. As the velocity of contraction increases tension decreases.
Expiratory flow limitation

PIF (faster contraction)
Operating Lung Volumes and Respiratory Effort

NEUROMECHANICAL DISSOCIATION

NORMAL

COPD

Corollary Discharge
Motor Output (RND)
Ventilatory Response

Feedback
Fig. 6. Breathlessness intensity as a function of pleural pressure expressed as a fraction of maximal inspiratory pressure (Ppl/MIP), inspiratory flow (V̇i), tidal volume expressed as a fraction of VC (Vt/VC), inspiratory time as a fraction of total respiratory cycle (Ti/Ttot), and breathing frequency (fb) using a multiple regression analysis.
Dyspnea and PImax

Borg dyspnea score (0-10)

1 = PImax < 40 cmH₂O
2 = PImax 40-80 cmH₂O
3 = PImax > 80 cmH₂O

50% predicted exercise capacity

FEV₁ > 80% pred
FEV₁ 40-80% pred
FEV₁ <40% pred

Killian KJ and Lones NL. Clinics in Chest Medicine, 1988
Development of respiratory muscle fatigue

Adapted from: Bellemare F and Grassino A, J. Appl. Physiol. 1982
Exercise limitation in Cardiorespiratory Disease

LUNGS and AIRWAYS

CARDIOCIRCULATORY

RESPIRATORY MUSCLES

PERIPHERAL MUSCLES

MOTIVATION
ANXIETY
FEAR

Exercise limitation in COPD

LUNGS AND AIRWAYS

- Expiratory Flow Limitation $\rightarrow$ Dynamic Hyperinflation
- Limit on tidal volume expansion $\rightarrow$ Rapid shallow breathing

Increases elastic mechanical loads ($PI \uparrow$)

RESPIRATORY MUSCLES

- Reduced $P_{I\text{max}}$ is prevalent ($P_{I\text{max}} \downarrow$)
- Functional weakening during exercise ($P_{I\text{max}} \downarrow$)
- Contribute to rapid shallow breathing ($PI \uparrow$)

Macklem PT, *ERJ* 2010
Exercise limitation in CHF

**LUNGS AND AIRWAYS**
- Decreased lung compliance
- Increased ventilatory needs

**RESPIRATORY MUSCLES**
- Reduced PImax is prevalent ($P_{\text{Imax}} \downarrow$)
- Reduced endurance capacity prevalent
- Functional weakening during exercise ($P_{\text{Imax}} \downarrow$)

Wong E. Heart, Lung and Circulation 2011;20:289-294
Campbell Diagram
Inspiratory Muscle Work

### Effects of IMT on breathing against resistance

<table>
<thead>
<tr>
<th></th>
<th>IMT (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (F/M)</td>
<td>5/5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>64 ± 5</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>22.6 ± 6.6</td>
</tr>
<tr>
<td>Plmax (cmH₂O)</td>
<td>67 ± 17</td>
</tr>
<tr>
<td>Plmax (%pred)</td>
<td>67 ± 10</td>
</tr>
<tr>
<td>Intensity endurance test (%Plmax)</td>
<td>50 ± 11</td>
</tr>
<tr>
<td>Endurance time (sec)</td>
<td>219 ± 71</td>
</tr>
<tr>
<td>Ti/Ttot (duty cycle) %</td>
<td>37±6</td>
</tr>
<tr>
<td>FEV₁ (%pred)</td>
<td>60 ± 17</td>
</tr>
<tr>
<td>FVC (%pred)</td>
<td>91 ± 16</td>
</tr>
<tr>
<td>FRC (%pred)</td>
<td>165 ± 45</td>
</tr>
</tbody>
</table>

Respiratory muscle load during resistive breathing task

Changes during endurance breathing test
Results: Inspiratory muscle function

<table>
<thead>
<tr>
<th></th>
<th>TFRL (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ PImax (cmH$_2$O)</td>
<td>+31 ± 4 *</td>
</tr>
<tr>
<td>Δ Duration E-test (sec)</td>
<td>+532 ± 204*</td>
</tr>
<tr>
<td>Δ Total work (J)</td>
<td>+407 ± 230*</td>
</tr>
<tr>
<td>Δ Avg. Peak inspiratory flow (L/sec)</td>
<td>+1.4 ± 0.6*</td>
</tr>
<tr>
<td>Δ Avg. Inspiratory time; Ti (sec)</td>
<td>-1.1 ± 0.8*</td>
</tr>
<tr>
<td>Δ Ti/Ttot; duty cycle (%)</td>
<td>-16 ± 6*</td>
</tr>
</tbody>
</table>

* indicates a statistically significant increase within group (p<0.05).

Respiratory muscle load during resistive breathing task

Changes during endurance breathing test

Pre-training

Post-training

Critical zone

NO FATIGUE

FATIGUE

Respiratory muscle load during resistive breathing task

Bellemare F and Grassino A, J. Appl. Physiol. 1982
The addition of TRFL-IMT to a PR program might have the following effects:

1) enhancement of the maximal velocity of shortening of the inspiratory muscle against high resistances would enable patients to shorten their inspiratory time and leave more time for expiration during exercise.

2) enhancement of inspiratory muscle function would result in improvements in $V_T$ expansion at identical levels of ventilation during exercise, by providing a training stimulus within the IRV

Aim of the study

To compare changes in breathing pattern at identical levels of ventilation during exercise after a TRRL-IMT and PR, and after PR alone in COPD patients with inspiratory muscle weakness.
## Results

### Baseline Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>IMT Group (n=25)</th>
<th>Control Group (n=25)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (F/M)</td>
<td>13/12</td>
<td>13/12</td>
<td>-</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66±6</td>
<td>66±7</td>
<td>0.882</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>26±6</td>
<td>24±6</td>
<td>0.315</td>
</tr>
<tr>
<td>FEV(_1) (%pred)</td>
<td>51±17</td>
<td>48±21</td>
<td>0.540</td>
</tr>
<tr>
<td>FEV(_1)/FVC (%)</td>
<td>45±16</td>
<td>44±13</td>
<td>0.860</td>
</tr>
<tr>
<td>Pmax (cmH(_2)O)</td>
<td>65±13</td>
<td>65±13</td>
<td>0.974</td>
</tr>
<tr>
<td>Pmax (%pred)</td>
<td>65±12</td>
<td>65±15</td>
<td>0.981</td>
</tr>
<tr>
<td>VO(_2)max (%pred)</td>
<td>68±23</td>
<td>71±32</td>
<td>0.699</td>
</tr>
<tr>
<td>Peak work rate (%pred)</td>
<td>50±24</td>
<td>55±21</td>
<td>0.529</td>
</tr>
<tr>
<td>6MWD (% pred)</td>
<td>65±19</td>
<td>66±22</td>
<td>0.827</td>
</tr>
</tbody>
</table>

Charususin et al. EUROPEAN RESPIRATORY JOURNAL VOL 47 ISSUE 4 – APRIL 2016
Results

Changes in inspiratory muscle function, exercise capacity and dyspnea

<table>
<thead>
<tr>
<th>Variables</th>
<th>IMT Group (n=25)</th>
<th>Control Group (n=25)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ PImax (cmH₂O)</td>
<td>+29±15*</td>
<td>+1±12</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Δ PImax (%pred)</td>
<td>+30±18*</td>
<td>+1±12</td>
<td>0.000</td>
</tr>
<tr>
<td>Δ PIF (L/sec)</td>
<td>+0.8±0.7*</td>
<td>-0.3±0.8</td>
<td>0.005</td>
</tr>
<tr>
<td>Δ Peak work rate (Watts)</td>
<td>+13±14*</td>
<td>+2±12</td>
<td>0.004</td>
</tr>
<tr>
<td>Δ Peak Vₑ (L/min)</td>
<td>+3±6*</td>
<td>-2±7</td>
<td>0.013</td>
</tr>
<tr>
<td>Δ Dyspneoa score after cycle test</td>
<td>+0.0±2.4</td>
<td>-0.0±1.5</td>
<td>0.201</td>
</tr>
<tr>
<td>Δ 6MWD (m)</td>
<td>+65±54*</td>
<td>+39±77*</td>
<td>0.164</td>
</tr>
<tr>
<td>Δ Dyspnea score after 6MWD</td>
<td>-0.6±1.9</td>
<td>-0.8±2.4</td>
<td>0.820</td>
</tr>
</tbody>
</table>

Δ 6MWD = 26 m

Charususin et al. EUROPEAN RESPIRATORY JOURNAL VOL 47 ISSUE 4 – APRIL 2016
Results: Breathing pattern

Changes in tidal volume ($V_T$), breathing frequency ($f_R$) at the comparable percentages of baseline $V_{E_{\text{max}}}$ (40, 60, 80, 100 and peak ventilation) at baseline and after training in control group.

Values represented as mean ± SEM.
Results: Breathing pattern

Changes in inspiratory flow ($V_{T}/Ti$) and inspiratory duty cycle ($Ti/Ttot$) at the comparable percentages of baseline $V_{E_{max}}$ (40, 60, 80, 100 and peak ventilation) at baseline and after training in IMT group.

Values represented as mean±SEM.
Conclusions

• Patients in the IMT group achieved significantly higher peak work rate and exercise ventilation without increasing dyspnea sensation at peak exercise.

• Favorable changes in breathing pattern (deeper and slower breathing) at iso-ventilation during exercise were only observed in the IMT group.

Charususin N, Gosselink R, McConnell AKM, Demeyer H, Topalovic M, Decramer M, Langer D. Inspiratory muscle training improves breathing pattern during exercise in COPD patients.

*European Respiratory Journal*, DOI: 10.1183/13993003.01574-2015

*ClinicalTrials.gov Identifier: NCT02186340*
Development of respiratory muscle fatigue

Changes during maximal cycle test

Bellemare F and Grassino A, J. Appl. Physiol. 1982

Pre-training

Post-training

NO FATIGUE

FATIGUE

Critical zone
IMT and dyspnea during exercise

- Compare effects of IMT on sensory and physiological responses to exercise in patients with COPD and respiratory muscle weakness randomized to 8-weeks of IMT or sham training.
Hypotheses

- Eight weeks of high intensity IMT (but not sham training) will delay the onset of intolerable dyspnea and improve exercise endurance in selected patients with COPD who have inspiratory muscle weakness.

- Improvements in dyspnea and exercise intolerance will be associated with improvements in inspiratory muscle function and attendant reduction in respiratory muscle effort and respiratory neural drive during exercise following IMT but not with sham training.
Training
Variable Flow Resistive IMT

- 8 weeks
- 2-3 daily sessions 30 breaths (4-5 min)
- 1 session / week supervised
- High intensity (Borg Effort 4-5/10)
- Placebo: <10% Pi,max
Endurance Cycling Task

Measurements:
- Operating lung volumes
- Ventilation
- Breathing pattern
- Gas exchange

Every (2) minute(s)

Shortness of Breath
Modified Borg Dyspnea Scale

- 0 Nothing at all
- 0.5 Very, very slight (just noticeable)
- 1 Very slight
- 2 Slight
- 3 Moderate
- 4 Somewhat Severe
- 5 Severe
- 6
- 7 Very Severe
- 8
- 9 Very, very severe (almost maximal)
- 10 Maximal

Flow

Volume

Endurance Cycling Task
Pes = Esophageal Pressure
Pga = Gastric Pressure
Pdi = Transdiaphragmatic Pressure
EMGdi = Diaphragmatic Electromyogram

## Baseline Characteristics (1)

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=10)</th>
<th>Sham (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male : Female, n</td>
<td>4 : 6</td>
<td>3 : 7</td>
</tr>
<tr>
<td>Age, years</td>
<td>73 ± 4</td>
<td>67 ± 7</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.1 ± 4.5</td>
<td>25.0 ± 6.8</td>
</tr>
<tr>
<td>Baseline Dyspnea Index score (0-12)</td>
<td>5.9 ± 1.5</td>
<td>4.7 ± 1.5</td>
</tr>
<tr>
<td>MRC Dyspnea (1-5)</td>
<td>2.9 ± 1.0</td>
<td>3.0 ± 1.1</td>
</tr>
<tr>
<td>Oxygen Cost Diagram (0-100)</td>
<td>54 ± 14</td>
<td>56 ± 11</td>
</tr>
</tbody>
</table>

**Post-bronchodilator pulmonary function:**

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=10)</th>
<th>Sham (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, L (% predicted)</td>
<td>1.04 ± 0.34 (52)</td>
<td>0.90 ± 0.30 (40)</td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>37 ± 12</td>
<td>33 ± 12</td>
</tr>
<tr>
<td>IC, L (% predicted)</td>
<td>1.67 ± 0.48 (72)</td>
<td>1.79 ± 0.66 (72)</td>
</tr>
<tr>
<td>FRC, L (% predicted)</td>
<td>4.02 ± 1.43 (136)</td>
<td>4.32 ± 1.16 (146)</td>
</tr>
<tr>
<td>RV, L (% predicted)</td>
<td>2.82 ± 1.30 (126)</td>
<td>3.25 ± 1.07 (155)</td>
</tr>
<tr>
<td>TLC, L (% predicted)</td>
<td>5.70 ± 1.52 (107)</td>
<td>6.11 ± 1.36 (113)</td>
</tr>
<tr>
<td>IC/TLC, %</td>
<td>30 ± 8</td>
<td>30 ± 10</td>
</tr>
<tr>
<td>D_LCo, mL/mm/mmHg (% predicted)</td>
<td>8.0 ± 2.9 (43)</td>
<td>7.9 ± 3.6 (40)</td>
</tr>
<tr>
<td>CLst, L/cmH2O</td>
<td>0.39 ± 0.24</td>
<td>0.38 ± 0.18</td>
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</table>
# Baseline Characteristics (2)

<table>
<thead>
<tr>
<th>Inspiratory Muscle Function:</th>
<th>Intervention (n=10)</th>
<th>Sham (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pi,\text{max}, \text{cmH}_2\text{O}</td>
<td>60 ± 11</td>
<td>60 ± 15</td>
</tr>
<tr>
<td>Load Endurance Test, % Pi,\text{max}</td>
<td>60 ± 9</td>
<td>65 ± 23</td>
</tr>
<tr>
<td>Endurance Time Baseline (min)</td>
<td>4.2 ± 1.1</td>
<td>3.9 ± 2.1</td>
</tr>
<tr>
<td>Total Work (J)</td>
<td>112 ± 62</td>
<td>124 ± 95</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exercise Capacity:</th>
<th>Intervention (n=10)</th>
<th>Sham (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak VO\text{2}, L/min</td>
<td>0.93 ± 0.23</td>
<td>0.95 ± 0.38</td>
</tr>
<tr>
<td>Peak Workrate, Watt (%predicted)</td>
<td>51 ± 23 (62)</td>
<td>49 ± 18 (47)</td>
</tr>
<tr>
<td>Workrate Endurance Test, % peak</td>
<td>69 ± 6</td>
<td>67 ± 12</td>
</tr>
<tr>
<td>Endurance Time Baseline (min)</td>
<td>7.3 ± 4.3</td>
<td>5.9 ± 2.4</td>
</tr>
<tr>
<td>Ventilation @ tlim, L (% MVV)</td>
<td>32.2 ± 7.7 (78)</td>
<td>31.8 ± 11.9 (84)</td>
</tr>
</tbody>
</table>
Training Intensity and Compliance

![Graph showing training intensity and compliance over weeks.](image)

**Intervention**
- Week 1: 94±8%
- Week 2: 99±2%
- Week 3: 99±2%
- Week 4: 95±12%
- Week 5: 93±14%
- Week 6: 97±6%
- Week 7: 87±25%
- Week 8: 99±2%
- Week 9: 100%
- Week 10: 100%

**Sham**
- Week 1: 95±11%
- Week 2: 92±17%
- Week 3: 94±10%
- Week 4: 99±2%
- Week 5: 100%
- Week 6: 100%
- Week 7: 100%
- Week 8: 100%

**Training Intensity**
- % Pi,max Baseline

**Training Week**

*Note: The graph shows the percentage of Pi,max baseline intensity over the course of training weeks for both intervention and sham groups.*
Total Work

Total Work per session (% Peak Work Baseline)

- Intervention
- Sham

Training Week

## Results

<table>
<thead>
<tr>
<th></th>
<th>Intervention n=9</th>
<th>Sham n=10</th>
<th>p-value</th>
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<tbody>
<tr>
<td><strong>Dyspnea and Inspiratory Muscle Function:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\Delta \Pi_{\text{imax}}$, cmH$_2$O</td>
<td>+ 18 ± 12</td>
<td>+ 6 ± 8</td>
<td>0.023</td>
</tr>
<tr>
<td>$\Delta \text{IM Endurance, min}$</td>
<td>+ 8.4 ± 4.1</td>
<td>+ 1.8 ± 2.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Transitional Dyspnea Index (-9 to 9)</td>
<td>+ 4.6 ± 2.2</td>
<td>+ 1.2 ± 3.2</td>
<td>0.017</td>
</tr>
<tr>
<td><strong>Exercise capacity:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\Delta \text{Tlim @75% Peak Workrate, min}$</td>
<td>+ 4.8 ± 5.1</td>
<td>+ 0.7 ± 1.3</td>
<td>0.031</td>
</tr>
</tbody>
</table>
Dyspnea

Sham

Intervention

Borg Dyspnea (0-10)

Baseline
8weeks
Rest

Baseline
8weeks
Rest

* *
Inspiratory Effort and RND

Sham

Intervention

Pes,tid (%Pes,max)

EMGdi / EMGdi,max
Conclusions

- Good compliance with home based IMT program
- Significant improvements in inspiratory muscle function
- Clinically relevant effects on dyspnea and cycle endurance accompanied by reduced respiratory effort (Pes/Pesmax) and respiratory neural drive (EMGdi) during exercise.
- IMT enables inspiratory muscles to perform identical task more efficiently probably resulting in less motor unit recruitment and reduced neural drive which might be mechanistically linked to improvements in neuromechanical coupling and dyspnea perception.
BREATHLESSNESS

Intensity

Quality

Cortex

Neural Respiratory Drive

Measure: Modified Borg

Measure: EMGdi/EMGdi,max

Healthy (exercise)

Lung disease

Obesity

Heart failure

Other conditions (e.g., anemia, hypoxia, altitude, aging)

Respiratory muscle weakness

Capacity of Respiratory Muscles

Respiratory Muscles

Load on Respiratory Muscles

Published in: Caroline J. Jolley; John Moxham; Am J Respir Crit Care Med 2016: 193, 236-238.
• Contribution of load / capacity imbalance of respiratory muscles to dyspnea and exercise limitation

• Interaction between work of breathing and peripheral muscle fatigue during exercise
Effect of respiratory muscle work on exercise performance: mechanisms

RESPIRATORY MUSCLE METABOREFLEX

- ↑ Sympathetic efferent discharge
- ↑ Limb vasoconstriction
- ↓ O₂ transport
- ↑ Locomotor muscle fatigue
- ↑ Effort perceptions

- Fatiguing contractions of the diaphragm, expiratory and accessory respiratory muscles
- ↑ Reflex activating metabolites
- ↑ Group III/IV phrenic afferent discharge

Dempsey et al, Respir Physiol Neuribiol, 2002
Inspiratory Muscles and Exercise Limitation

Inspiratory Muscles and Exercise Limitation

Inspiratory Muscles and Exercise Limitation

**Forearm Blood Flow**

- **Healthy**
- **CHF**

**Graph Details**
- **Y-axis**: Forearm Blood Flow (ml/min/100ml)
- **X-axis**: EndIL, 1min, 2min, EndHGE

Chiappa, G. R. et al. J Am Coll Cardiol 2008;51:1663-1671
Inspiratory Muscles and Exercise Limitation

C

Potentiated quadriceps twitch force expressed as a percentage of preexercise baseline before and 10 and 35 min after exercise.
Conclusions

- Imbalance between increased neural drive (i.e. increased load) and inappropriate musculo-mechanical response results in dyspnea
- Neuromechanical Dissociation
- Increasing capacity of respiratory muscles delays onset of dyspnea symptoms during exercise
- Decreased respiratory muscle work during exercise related with less peripheral muscle fatigue and improved exercise capacity
- Role of increasing respiratory capacity by IMT on peripheral muscle fatigue needs to be established