Respiratory Muscle Training in Congestive Heart Failure?!

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Most important factors contributing to skeletal muscle impairment in COPD and CHF

Fig. 1. Most important factors contributing to skeletal muscle impairment in chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF).

The physiological basis of rehabilitation in chronic heart and lung disease
Muscle hypothesis in CHF

Coats et al, 1994
Respiratory Metaboreflex ("Steal Effect")

Increased ventilation and skeletal and respiratory myopathy in CHF

Hypothesis

High Energy + Circulatory Demand by Sustained Hyperventilation (Up to ~14-16% of Total VO₂, CO)
  ↓ Diaphragm, Accessory Muscle Fatigue
  ↓ Activate Respiratory Muscles Metaboreflex = ↑ Sympathetic Outflow
  ↓ Locomotor Muscle Vasoconstriction, ↓ \( Q_{\text{imb}} \)
  ↓ Locomotor Muscle Fatigue + ↑ Effort Perception
  ↓ Endurance Performance
  ↓ Relevance to CHF ...to COPD?

Respiratory Muscle Metaboreflex at ~ 60%Pi-max


- ↑ Sympathetic efferent discharge, Limb vasoconstriction
- ↓ \( O_2 \) transport
- ↑ Locomotor muscle fatigue
- Intensify effort perceptions

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

Summarized: Increased ventilation (VE/VCO₂-slope)

High VE/VCO₂ slope

- Functional high VD/VT ratio
  - Lung restrictive pattern
  - Reduced alveolar-capillary membrane diffusion
  - Ventilation-perfusion mismatch

- Early lactic acidosis
  - Reduced cardiac output
  - Muscle deconditioning
  - Increased type IIB muscular fibre expression

- Impaired breathing control
  - Peripheral and/or central chemoreflex deregulation
  - Ergoreceptor activation
  - Central nervous system and hormone influence

Exercise periodic breathing

Figure 1  Mechanisms involved in the genesis of increased VE/VCO₂ slope and EPB. PaCO₂, arterial partial pressure of CO₂; for details see text.

European Heart Journal (2007) 28, 673-678
# Respiratory Muscle function in CHF

~30% patients with CHF have respiratory muscle weakness

(Chiappa et al, 2008)

## Table 3  Respiratory muscle function in chronic heart failure

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>MIP</th>
<th>MEP</th>
<th>Correlation with exercise capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hammond et al.</strong></td>
<td>16</td>
<td>↓</td>
<td>↓</td>
<td></td>
</tr>
<tr>
<td><strong>McParland et al.</strong></td>
<td>9</td>
<td>↓</td>
<td>↓</td>
<td></td>
</tr>
<tr>
<td><strong>Evans et al.</strong></td>
<td>20</td>
<td>↓</td>
<td>↓</td>
<td>Yes (MIP and Mahler dyspnoea index)</td>
</tr>
<tr>
<td><strong>Ambrosino et al.</strong></td>
<td>45</td>
<td>↓</td>
<td>↓</td>
<td>No</td>
</tr>
<tr>
<td><strong>Chua et al.</strong></td>
<td>20</td>
<td>↓</td>
<td></td>
<td>Yes (MIP and peak VO$_2$)</td>
</tr>
<tr>
<td><strong>Mancini et al.</strong></td>
<td>10</td>
<td></td>
<td></td>
<td>(Trend to ↓)</td>
</tr>
<tr>
<td><strong>Mancini et al.</strong></td>
<td>15</td>
<td></td>
<td></td>
<td>(Trend to ↓)</td>
</tr>
<tr>
<td><strong>Nishimura et al.</strong></td>
<td>23 (In NYHA III/IV)</td>
<td></td>
<td></td>
<td>Yes (MIP and peak VO$_2$)</td>
</tr>
</tbody>
</table>

MIP = maximum inspiratory pressure, MEP = maximum expiratory pressure.

*European Heart Journal* (1997) 18, 1865–1872
Respiratory Muscles and prognosis in CHF

Survival (%)

Follow-Up Period (Months)

P_{imax} Quartiles
Q1: >9.8 kPa
Q2: >7.5 to ≤9.8 kPa
Q3: >5.3 to ≤7.5 kPa
Q4: ≤5.3 kPa

P=0.014

> 100 cm H_2O

< 55 cm H_2O
$P_{i\text{-}max}$ for prediction of survival at 12 months

AUC = 0.82

AUC = 0.68

Circulation. 2001 May 1;103(17):2153-8
Ventilatory efficiency (VE/VCO_2) and survival

Fig. 1. Kaplan-Meier curves for patients achieving ≥33 or < 33 for the lowest minute ventilation (VE) and carbon dioxide production (VCO_2) ratio (P < .01). Numbers given along the curves are cumulative numbers of composite outcomes; numbers in parentheses are patients evaluated at each time point.
Evidence of IMT in CHF

Efficacy of inspiratory muscle training in chronic heart failure patients: A systematic review and meta-analysis

Table 2
Summary of included study designs.

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Control</th>
<th>Exercise Program</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosnak-Gudu 2011 [12]</td>
<td>40% PI (n = 16)</td>
<td>15% PI (n = 14)</td>
<td>30 mins, 7 days week⁻¹, 6 weeks 6 home sessions, 1 hospital session</td>
<td>PIₓₓₓ, 6 MWD, QOL</td>
</tr>
<tr>
<td>Dall’ Ago 2006 [7]</td>
<td>30% PI (n = 16)</td>
<td>0% PI (n = 16)</td>
<td>30 mins, 7 days week⁻¹, 12 weeks 6 home sessions, 1 hospital session</td>
<td>PIₓₓₓ, Peak VO₂, 6MWD, V̇E/VCO₂, QOL</td>
</tr>
<tr>
<td>Johnson 1998 [13]</td>
<td>30% PI (n = 9)</td>
<td>15% PI (n = 9)</td>
<td>30 mins, 7 days week⁻¹, 6 weeks 6 home sessions, 1 hospital session</td>
<td>PIₓₓₓ, QOL</td>
</tr>
<tr>
<td>Laoutaris, 2004 [14]</td>
<td>60% PI (n = 20)</td>
<td>15% PI (n = 15)</td>
<td>To fatigue, 3 days week⁻¹, 10 weeks All sessions at hospital</td>
<td>PIₓₓₓ, Peak VO₂, 6MWD, V̇E/VCO₂, VT, LVEF, QOL</td>
</tr>
<tr>
<td>Laoutaris, 2007 [15]</td>
<td>60% PI (n = 15)</td>
<td>15% PI (n = 23)</td>
<td>To fatigue, 3 days week⁻¹, 10 weeks All sessions at hospital</td>
<td>PIₓₓₓ, Peak VO₂, 6MWD, VT, V̇E/VCO₂</td>
</tr>
<tr>
<td>Laoutaris, 2008 [16]</td>
<td>60% PI (n = 14)</td>
<td>15% PI (n = 9)</td>
<td>To fatigue, 3 days week⁻¹, 10 weeks All sessions at hospital</td>
<td>PIₓₓₓ, Peak VO₂, QOL, VT, V̇E/VCO₂</td>
</tr>
<tr>
<td>Laoutaris 2011 [17]</td>
<td>60% PI (n = 10)</td>
<td>(n = 5)</td>
<td>To fatigue, 3 days week⁻¹, 10 weeks All IMT sessions at hospital Both groups walked 30–45 min day⁻¹</td>
<td>PIₓₓₓ, Peak VO₂, 6MWD, QOL, V̇E/VCO₂</td>
</tr>
<tr>
<td>Martinez, 2001 [18]</td>
<td>Max. PI (n = 11)</td>
<td>10% PI (n = 9)</td>
<td>2x15 mins, 6 days week⁻¹, 6 weeks 5 home sessions, 1 hospital session</td>
<td>PIₓₓₓ, Peak VO₂, 6MWD, LVEF</td>
</tr>
<tr>
<td>Padula 2009 [8]</td>
<td>30% PI (n = 15)</td>
<td>Education (n = 17)</td>
<td>10-20 mins, 7 days week⁻¹, 12 weeks All home sessions with nurse coaching</td>
<td>PIₓₓₓ, Bandura-Self Efficacy</td>
</tr>
<tr>
<td>Weiner, 1999 [19]</td>
<td>60% PI (n = 10)</td>
<td>0% PI (n = 10)</td>
<td>30 mins, 6 days week⁻¹, 12 weeks All supervised by physiotherapist</td>
<td>PIₓₓₓ, Peak VO₂, 12 MWD, LVEF</td>
</tr>
<tr>
<td>Winklemann, 2009 [6]</td>
<td>30% PI (n = 12) Aerobic Ex.</td>
<td>(n = 12) Aerobic Ex</td>
<td>Respiration 30 mins, 7 days week⁻¹ 6 home sessions, 1 hospital session Aerobic 12 weeks, 3 days wk⁻¹, 45 min</td>
<td>PIₓₓₓ, V̇E/VCO₂, Peak VO₂, 6MWD, QOL</td>
</tr>
</tbody>
</table>

6 MWD = 6 Minute Walk Distance.
QOL = Quality of life (Minnesota questionnaire).
LVEF = Left Ventricular Ejection Fraction (%).
PIₓₓₓ = Maximal inspiratory pressure.
V̇E/VCO₂ = Ventilatory equivalent slope for carbon dioxide.
VT = Ventilatory Threshold.

IMT in CHF: Strength ($P_{i\text{-max}}$)

$P_{i\text{max}} = +20 \text{ cmH}_2\text{O (95\% C.I. 13,9 -- 26,1)}$

IMT in CHF: Ventilatory efficiency ($\text{VE/}V\text{CO}_2$)

$V_E/V\text{CO}_2$: -2.28 (95% C.I. -3.25 to -1.30)

**IMT in CHF: Cardiorespiratory Fitness (VO$_{2\text{-peak}}$)**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dall’Ago 2006</td>
<td>3.8</td>
<td>3.9</td>
<td>16</td>
<td>0.1</td>
<td>0.19</td>
<td>16</td>
<td>6.7%</td>
<td>3.70 [1.79, 5.61]</td>
</tr>
<tr>
<td>Laoutaris 2004</td>
<td>2.4</td>
<td>3</td>
<td>20</td>
<td>0.1</td>
<td>0.18</td>
<td>15</td>
<td>14.1%</td>
<td>2.30 [0.98, 3.62]</td>
</tr>
<tr>
<td>Laoutaris 2007</td>
<td>2.1</td>
<td>2.73</td>
<td>15</td>
<td>-0.9</td>
<td>2.08</td>
<td>23</td>
<td>9.3%</td>
<td>3.00 [1.38, 4.62]</td>
</tr>
<tr>
<td>Laoutaris 2008</td>
<td>1.9</td>
<td>3.6</td>
<td>14</td>
<td>-0.4</td>
<td>9.25</td>
<td>9</td>
<td>0.6%</td>
<td>2.30 [-4.03, 8.63]</td>
</tr>
<tr>
<td>Laoutaris 2011</td>
<td>2.5</td>
<td>2.33</td>
<td>10</td>
<td>-0.1</td>
<td>0.3</td>
<td>5</td>
<td>11.3%</td>
<td>2.60 [1.13, 4.07]</td>
</tr>
<tr>
<td>Martinez 2001</td>
<td>2.6</td>
<td>3.85</td>
<td>11</td>
<td>2.6</td>
<td>2.86</td>
<td>9</td>
<td>2.8%</td>
<td>0.00 [-2.94, 2.94]</td>
</tr>
<tr>
<td>Weiner 1999</td>
<td>0.7</td>
<td>0.84</td>
<td>10</td>
<td>-0.5</td>
<td>0.7</td>
<td>10</td>
<td>53.2%</td>
<td>1.20 [0.52, 1.88]</td>
</tr>
<tr>
<td>Winkelmann 2009</td>
<td>4.6</td>
<td>3.59</td>
<td>12</td>
<td>3.1</td>
<td>4.88</td>
<td>12</td>
<td>2.1%</td>
<td>1.50 [-1.93, 4.93]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>108</td>
<td></td>
<td>99</td>
<td>100.0%</td>
<td>1.83</td>
<td>[1.33, 2.32]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi$^2 = 12.07$, df = 7 ($P = 0.10$); $I^2 = 42$
Test for overall effect: $Z = 7.24$ ($P < 0.000001$)

**Fig. 2.** Mean difference in peak VO$_2$, IMT versus control.

**VO$_{2\text{-peak}}$ = +1.83 ml/kg/min (~ 1 MET)**

(95% C.I. 1.33 – 2.23)
**IMT in CHF: Six Minute Walk distance**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Fixed, 95% CI</th>
<th>Mean Difference</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosnak-Gucu 2011</td>
<td>60</td>
<td>58.9</td>
<td>16</td>
<td>13.7</td>
<td>27.9</td>
<td>14</td>
<td>13.5%</td>
<td>46.30 [13.95, 78.65]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dall'Ago 2006</td>
<td>101</td>
<td>108.2</td>
<td>16</td>
<td>-21</td>
<td>39.4</td>
<td>16</td>
<td>4.4%</td>
<td>122.00 [65.58, 178.42]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laoutaris 2004</td>
<td>66.3</td>
<td>76.3</td>
<td>20</td>
<td>8.4</td>
<td>15.2</td>
<td>15</td>
<td>12.0%</td>
<td>57.90 [23.59, 92.21]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laoutaris 2007</td>
<td>26.1</td>
<td>33.2</td>
<td>15</td>
<td>8</td>
<td>18.5</td>
<td>23</td>
<td>41.7%</td>
<td>18.10 [-0.32, 36.52]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laoutaris 2011</td>
<td>65</td>
<td>55.7</td>
<td>10</td>
<td>18</td>
<td>18.9</td>
<td>5</td>
<td>9.7%</td>
<td>47.00 [8.71, 85.29]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Martinez 2001</td>
<td>35</td>
<td>54.8</td>
<td>11</td>
<td>19</td>
<td>24.7</td>
<td>9</td>
<td>10.8%</td>
<td>16.00 [-20.18, 52.18]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Winkelmann 2009</td>
<td>80</td>
<td>61.6</td>
<td>12</td>
<td>56</td>
<td>43.1</td>
<td>12</td>
<td>7.8%</td>
<td>24.00 [-18.54, 66.54]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>100</td>
<td></td>
<td>94</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>34.35 [22.45, 46.24]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 16.23, df = 6 (P = 0.01); I² = 63%
Test for overall effect: Z = 5.66 (P < 0.00001)

**Fig. 3.** Mean difference in six minute walk distance IMT versus control.

**6MWT= +34.4m (95% C.I. 22.45 – 46.24m)**

**MCID ~20-30 m (O’Keeffe et al, 1998)**
IMT in CHF: QoL

Fig. 4. Mean difference in Minnesota living with heart failure score, IMT versus control.

MLWHFQ = -12.25; 95% C.I. -17.08 to -7.43

IMT and IMW in CHF

Inspiratory Muscle Weakness

Montemezzo et al, 2014
## IMT and IMW in CHF

### Six minute walk distance

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean [meters]</th>
<th>SD [meters]</th>
<th>Total</th>
<th>Mean [meters]</th>
<th>SD [meters]</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI [meters]</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspiratory muscle weakness 1.1</td>
<td>1.01</td>
<td>0.17</td>
<td>16</td>
<td>0.21</td>
<td>0.41</td>
<td>16</td>
<td>0.342</td>
<td>80.00 [58.25, 101.75]</td>
<td>2008</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal inspiratory muscle strength 1.2</td>
<td>0.55</td>
<td>0.78</td>
<td>11</td>
<td>0.19</td>
<td>1.10</td>
<td>9</td>
<td>0.144</td>
<td>16.00 [-69.38, 101.38]</td>
<td>2001</td>
</tr>
<tr>
<td>Martinez AS, 2001</td>
<td>0.663</td>
<td>0.9972</td>
<td>20</td>
<td>0.84</td>
<td>0.9604</td>
<td>15</td>
<td>0.194</td>
<td>57.90 [-7.46, 123.26]</td>
<td>2004</td>
</tr>
<tr>
<td>Laoutaris I, 2007</td>
<td>0.261</td>
<td>0.4027</td>
<td>15</td>
<td>0.08</td>
<td>0.4795</td>
<td>23</td>
<td>0.321</td>
<td>18.10 [-10.17, 46.37]</td>
<td>2007</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>0.62</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable
Test for overall effect: Z = 7.21 (P < 0.00001)

Heterogeneity: Tau² = 0.00; Chi² = 1.23, df = 2 (P = 0.54); I² = 0%
Test for overall effect: Z = 1.87 (P = 0.06)

Heterogeneity: Tau² = 1167.36; Chi² = 12.42, df = 3 (P = 0.006); I² = 76%
Test for overall effect: Z = 2.22 (P = 0.03)
Test for subgroup differences: Chi² = 11.19, df = 1 (P = 0.001), P = 91.1%
IMT in IMW in HF

Peak oxygen consumption

Montemezzo et al, 2014
Conclusions of IMT in CHF

• Improves: RM strength and endurance; VO$_2$-peak; 6-MWD and QoL.

• Alternative to the more severity de-conditioned CHF patients who may than transition to conventional exercise training.

• Focus on patients with inspiratory muscle weakness!
FITT Principle Formula: 4 Variables

1. Frequency
2. Intensity
3. Time
4. Type

The values for each one change based on which Component of Fitness or activity they apply to.
Training Intensity

Figure 1. Average Training Efficiency Based on IMT Training Intensity
High Intensity IMT (2)

Figure 3 Progression of strength [maximal inspiratory pressure ($P_{\text{max}}$)] and endurance [10 maximal repetitions (RM)] during follow-up. IMT, inspiratory muscle training.

European Journal of Heart Failure (2013) 15, 892–901
Figure 4 - Maximal inspiratory pressure for treatment with inspiratory muscle training versus control groups. 

$P_{\text{max}}$ - maximal inspiratory pressure; IMT - inspiratory muscle training; CI - confidence interval; SD - standard deviation. 1.3.1 - $P_{\text{max}}$ for all studies; 1.3.2 - $P_{\text{max}}$ for studies that performed IMT for 6-8 weeks; 1.3.3 - $P_{\text{max}}$ for studies that performed IMT for 12 weeks.
### Figure 2 - Peak VO₂ for treatment with inspiratory muscle training versus control groups.

IMT - inspiratory muscle training; CI - confidence interval; SD - standard deviation. 1.1.1 – Peak VO₂ for all studies; 1.1.2 – Peak VO₂ for studies that performed IMT for 12 weeks.

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**Training Time: VO₂peak**

![Figure 2](image_url)
### Training Time: 6MWD

#### Figure 3 - Distance walked in the 6-MWT for treatment with inspiratory muscle training versus control groups.

**IMT** - inspiratory muscle training; CI - confidence interval; SD - standard deviation. 1.2.1 - Distance walked in the 6-MWT for all studies; 1.2.2 - Distance walked in the 6-MWT for studies that performed IMT for 6 weeks.
Exercise training and inspiratory metaboreflex (at 60% $P_{i\text{-max}}$)

**Figure 4.** Leg blood flow response, assessed by Doppler ultrasonography, during the induction of the inspiratory metaboreflex at 60% $P_{i\text{max}}$. Endurance trained subjects are represented by close circles and sedentary subjects are represented by open circles.

Jorge P. Ribeiro$^{1,2}$, Gaspar R. Chiappa$^1$, Carine C. Callegaro$^{1,3}$
IMT and Metaboreflex in CHF

N=18 CHF
LVEF < 40%
IMW: [PImax] < 70%pred

Figure 1: Hemodynamic Responses of the Resting Calf to Inspiratory Loading

Chiappa et al.
Inspiratory Muscle Training and Blood Flow
Any Questions... Just Ask!