CARDIOPULMONARY FUNCTION TEST: WHAT MAKES SENSE

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Exercise testing is increasingly used to assess the aerobic reserve of lung resection candidates.

These tests have the capability to assess the entire oxygen transport system and to detect possible deficits that may predispose to postoperative complications.

Therefore, the potential exists to evaluate much of the cardiopulmonary system with just one test

(Olsen GN. Chest 1989; 95: 218-225)
Types of exercise tests

Test low-tech:
• 6-min walking test
• Shuttle test
• Stair climbing test

Test high tech:
• VO2/VCO2 measurement (Cycle, treadmill)
Cardiopulmonary exercise test

- Performed in a controlled environment.
- Continuous monitoring of various parameters.
- Easy standardization and good reproducibility of results.
- PeakVO2 is the single most important parameter as a direct measure of exercise capacity.
- CPET does not only allow assessment of over-all cardio-pulmonary reserves, but in case of a limitation of exercise capacity, to find the reason for this, such as pulmonary, cardiovascular, or musculo-skeletal limitations.
VO2max and postop morbidity
Exercise Capacity as a Predictor of Postoperative Complications in Lung Resection Candidates

CHRIS T. BOLLIGER, PAUL JORDAN, MARKUS SOLER, PETER STULZ, ERICH GRADEL, KAREL SKARVAN, SERGE ELSASSER, MICHAEL GONON, CHRISTOPH WYSER, MICHAEL TAMM, and ANDRÉ P. PERRUCHOU

Division of Pneumology, Department of Internal Medicine, the University Computer Center, the Cardiothoracic Unit, Department of Surgery, and the Department of Anesthesiology, University Hospital, Basel, Switzerland
Exercise capacity and extent of resection as predictors of surgical risk in lung cancer


Table 3. – Results of stepwise logistic regression analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Step</th>
<th>Coeff</th>
<th>SEM</th>
<th>Improvement Chi-squared</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant factor</td>
<td>0</td>
<td>2.9883</td>
<td>1.2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>$V'O_2,\text{max}\cdot\text{kg body weight}^{-1} %\text{ pred}$</td>
<td>1</td>
<td>-0.0573</td>
<td>0.014</td>
<td>19.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Resection %</td>
<td>2</td>
<td>0.0343</td>
<td>0.015</td>
<td>5.3</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Table 4. – Probabilities of postoperative complications based on exercise tests and lung resection according to stepwise logistic regression analysis

<table>
<thead>
<tr>
<th>$V'O_2,\text{max} \cdot \text{kg body weight}^{-1} %\text{ pred}$</th>
<th>SE/wedge</th>
<th>LE</th>
<th>BLE</th>
<th>PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>0.03</td>
<td>0.04</td>
<td>0.07</td>
<td>0.11</td>
</tr>
<tr>
<td>110</td>
<td>0.04</td>
<td>0.07</td>
<td>0.12</td>
<td>0.17</td>
</tr>
<tr>
<td>100</td>
<td>0.08</td>
<td>0.11</td>
<td>0.19</td>
<td>0.27</td>
</tr>
<tr>
<td>90</td>
<td>0.13</td>
<td>0.19</td>
<td>0.29</td>
<td>0.39</td>
</tr>
<tr>
<td>80</td>
<td>0.21</td>
<td>0.29</td>
<td>0.42</td>
<td>0.53</td>
</tr>
<tr>
<td>70</td>
<td>0.31</td>
<td>0.42</td>
<td>0.56</td>
<td>0.67</td>
</tr>
<tr>
<td>60</td>
<td>0.45</td>
<td>0.56</td>
<td>0.69</td>
<td>0.78</td>
</tr>
<tr>
<td>50</td>
<td>0.59</td>
<td>0.69</td>
<td>0.80</td>
<td>0.86</td>
</tr>
</tbody>
</table>

6 of 7 pts with VO2 < 60% had compl (86%)
11 of 17 with VO2 < 15 ml/kg/min had compl (65%)
8 of 65 with VO2 > 90% had compl (12%)
• January 2006-June 2008: 263 CPET
• 59 wedge or segmentectomy
• 204 major resections (177 L, 27 P)
Respiratory complications by peakVO2 (204 anatomic resections)

Brunelli A et al. CHEST 2009
Mortality and peakVO2
(204 anatomic resections)

Brunelli A et al. CHEST 2009
Stratification of outcomes by peak VO2

Brunelli A et al. CHEST 2009
Benzo R et al. Respir Med 2007
<table>
<thead>
<tr>
<th></th>
<th>Area under the curve</th>
<th>SE</th>
<th>Lower-upper bound</th>
<th>p-value</th>
<th>Cut-off</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total morbidity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V'O_2$ kg$^{-1}$</td>
<td>0.717</td>
<td>0.045</td>
<td>0.651-0.777</td>
<td>0.0001</td>
<td>12.8</td>
<td>51</td>
<td>85</td>
</tr>
<tr>
<td>$V'O_2$ kg$^{-1}$ PBW</td>
<td>0.710</td>
<td>0.045</td>
<td>0.643-0.771</td>
<td>0.0001</td>
<td>15.8</td>
<td>64</td>
<td>69</td>
</tr>
<tr>
<td>$V'O_2$ % pred</td>
<td>0.657</td>
<td>0.045</td>
<td>0.589-0.722</td>
<td>0.0010</td>
<td>58</td>
<td>75</td>
<td>48</td>
</tr>
<tr>
<td>ASA score</td>
<td>0.593</td>
<td>0.039</td>
<td>0.523-0.661</td>
<td>0.0156</td>
<td>3</td>
<td>71</td>
<td>48</td>
</tr>
<tr>
<td>ppo FEV1</td>
<td>0.565</td>
<td>0.045</td>
<td>0.495-0.633</td>
<td>0.7880</td>
<td>64</td>
<td>65</td>
<td>49</td>
</tr>
<tr>
<td><strong>Cardiovascular complications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V'O_2$ kg$^{-1}$</td>
<td>0.708</td>
<td>0.065</td>
<td>0.640-0.771</td>
<td>0.0011</td>
<td>13.6</td>
<td>63</td>
<td>72</td>
</tr>
<tr>
<td>$V'O_2$ kg$^{-1}$ PBW</td>
<td>0.738</td>
<td>0.054</td>
<td>0.671-0.798</td>
<td>0.0001</td>
<td>16.2</td>
<td>75</td>
<td>61</td>
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<tr>
<td>$V'O_2$ % pred</td>
<td>0.633</td>
<td>0.061</td>
<td>0.562-0.700</td>
<td>0.0029</td>
<td>53</td>
<td>64</td>
<td>61</td>
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<tr>
<td>ASA score</td>
<td>0.630</td>
<td>0.046</td>
<td>0.560-0.695</td>
<td>0.0080</td>
<td>3</td>
<td>79</td>
<td>47</td>
</tr>
<tr>
<td>ppo FEV1 % pred</td>
<td>0.492</td>
<td>0.066</td>
<td>0.422-0.562</td>
<td>0.9030</td>
<td>80</td>
<td>29</td>
<td>79</td>
</tr>
<tr>
<td><strong>Pulmonary complications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V'O_2$ kg$^{-1}$</td>
<td>0.723</td>
<td>0.057</td>
<td>0.654-0.784</td>
<td>0.0001</td>
<td>12.3</td>
<td>56</td>
<td>86</td>
</tr>
<tr>
<td>$V'O_2$ kg$^{-1}$ PBW</td>
<td>0.691</td>
<td>0.065</td>
<td>0.580-0.718</td>
<td>0.0020</td>
<td>12.1</td>
<td>45</td>
<td>94</td>
</tr>
<tr>
<td>$V'O_2$ % pred</td>
<td>0.616</td>
<td>0.066</td>
<td>0.544-0.684</td>
<td>0.0169</td>
<td>37</td>
<td>30</td>
<td>95</td>
</tr>
<tr>
<td>ASA score</td>
<td>0.597</td>
<td>0.044</td>
<td>0.527-0.664</td>
<td>0.0269</td>
<td>3</td>
<td>73</td>
<td>47</td>
</tr>
<tr>
<td>ppo FEV1</td>
<td>0.545</td>
<td>0.051</td>
<td>0.480-0.614</td>
<td>0.3716</td>
<td>64</td>
<td>73</td>
<td>50</td>
</tr>
</tbody>
</table>

Quantification of Cardiorespiratory Fitness in Healthy Nonobese and Obese Men and Women

Santiago Lorenzo, Ph.D., and Tony G. Buck, Ph.D.
Quantification of Cardiorespiratory Fitness in Healthy Nonobese and Obese Men and Women

Santiago Lorenzo, Ph.D., and Tony G. Babh, Ph.D.

A. Equation R

\[ y = 0.197x + 74.158 \]

\[ r^2 = 0.091 \]

B. Equation W

\[ y = -0.053x + 93.518 \]

\[ r^2 = 0.010 \]

C. Equation G

\[ y = -0.062x + 98.657 \]

\[ r^2 = 0.011 \]
Effect of pre-operative training in lung cancer patients
Short term aerobic training. 4-6 sessions/week, 4-6 weeks + pt education and breathing techniques

Jones L Cancer 2007, 20 pts
Increase in peak VO2max (2.3 ml/kg/min)
Increase in 6MWT (40 m)
No changes in PFTs

Bobbio A EJCTS 2008, 12 pts

• Increase in peak VO2 (2.8mL/kg/min)
• No improvement of PFT

Divisi D EJCTS 2013, 27 pts

• Increase in peak VO2 (6.3 ml/kg/min)
• Increase in PaO2 (22 mmHg)
• Increase in PFTs (FEV1, FEV1/FVC)
7.4.3. In patients with lung cancer being considered for surgery and deemed at high risk (as defined by the proposed functional algorithm, ie, PPO \( FEV_1 \) or PPO \( DLCO < 60\% \) and \( Vo_2\max < 10 \text{ ml/kg/min} \) or <35\%), preoperative or postoperative pulmonary rehabilitation is recommended (Grade 1C).
Beyond VO2max: VE/VCO2
Exercise ventilatory inefficiency and mortality in patients with chronic obstructive pulmonary disease undergoing surgery for non-small-cell lung cancer

Roberto Torchio\textsuperscript{a,*}, Marco Guglielmo\textsuperscript{a}, Roberto Giardino\textsuperscript{b}, Francesco Ardissone\textsuperscript{b}, Claudio Ciacco\textsuperscript{a}, Carlo Gulotta\textsuperscript{e}, Aleksandar Veljkovic\textsuperscript{d}, Massimiliano Bugian\textsuperscript{e}

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>z</th>
<th>p &gt; z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V'<em>E/V'</em>\text{CO}_2$ slope</td>
<td>1.24</td>
<td>1.06–1.44</td>
<td>2.77</td>
<td>0.0060</td>
</tr>
<tr>
<td>BMI</td>
<td>0.75</td>
<td>0.55–1.04</td>
<td>−1.73</td>
<td>0.0830</td>
</tr>
<tr>
<td>Risk of complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V'_O_2$ peak</td>
<td>0.05</td>
<td>0.01–0.58</td>
<td>−2.39</td>
<td>0.0170</td>
</tr>
<tr>
<td>BMI</td>
<td>1.17</td>
<td>1.00–1.37</td>
<td>1.97</td>
<td>0.0490</td>
</tr>
</tbody>
</table>

VE/VCO2 slope < 34: 98% survival probability
VE/VCO2 slope≥34: 5.5% probability of death

c-index 0.87
Minute Ventilation-to-Carbon Dioxide Output (\(\dot{V}_E/\dot{V}_{CO_2}\)) Slope Is the Strongest Predictor of Respiratory Complications and Death After Pulmonary Resection

Alessandro Brunelli, MD, Romualdo Belardinelli, MD, Cecilia Pompili, MD, Francesco Xiumé, MD, Majed Refai, MD, Michele Salati, MD, and Armando Sabbatini, MD
VE/VCO2 is a predictor of respiratory complications either in pts with VO2<15 and VO2>15 mL/kg/min
VE/VCO2 is a predictor of respiratory complications either in pts with and without COPD

VE/VCO2 > vs. < 35: RC 22% vs 7.6%; death 7.6% vs. 0.2%
CPET and cardiac risk
Exercise-induced myocardial ischaemia detected by cardiopulmonary exercise testing

Romualdo Belardinelli\textsuperscript{a\#}, Francesca Lacalaprice\textsuperscript{a}, Flavia Carle\textsuperscript{b}, Adelaide Minucci\textsuperscript{b}, Giovanni Cianci\textsuperscript{a}, GianPiero Perna\textsuperscript{a}, Giuseppe D'Eusanio\textsuperscript{a}
VO2max AND survival
**Overall Survival**

<table>
<thead>
<tr>
<th>PREDICTORS</th>
<th>HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age&gt;70</td>
<td>2.3</td>
<td>0.005</td>
</tr>
<tr>
<td>VO2max&lt;60%</td>
<td>2.4</td>
<td>0.001</td>
</tr>
</tbody>
</table>

P=0.0004

Cancer specific Survival

P=0.01

VO2max AND quality of life after surgery
Quality of life after lung resection is not associated with functional objective measures

<table>
<thead>
<tr>
<th>Postop QoL scale</th>
<th>VO\textsubscript{2}max &gt; 15 mL/kg/min [155]</th>
<th>VO\textsubscript{2}max &lt; 15 mL/kg/min [66]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCS</td>
<td>49.7 [7.6]</td>
<td>47.7 [8.1]</td>
<td>0.1</td>
</tr>
<tr>
<td>MCS</td>
<td>49.1 [10.4]</td>
<td>46.3 [12.3]</td>
<td>0.2</td>
</tr>
<tr>
<td>PF</td>
<td>50 [7.6]</td>
<td>44.5 [9.7]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RP</td>
<td>45 [11.4]</td>
<td>44 [12.5]</td>
<td>0.6</td>
</tr>
<tr>
<td>BP</td>
<td>51.1 [10.5]</td>
<td>52.6 [9.9]</td>
<td>0.3</td>
</tr>
<tr>
<td>GH</td>
<td>49.1 [8.6]</td>
<td>46.5 [9.7]</td>
<td>0.09</td>
</tr>
<tr>
<td>VT</td>
<td>56.1 [8.9]</td>
<td>52.1 [10.7]</td>
<td>0.006</td>
</tr>
<tr>
<td>SF</td>
<td>48.6 [10]</td>
<td>46.6 [10.3]</td>
<td>0.2</td>
</tr>
<tr>
<td>RE</td>
<td>46.5 [12.7]</td>
<td>45.1 [13.2]</td>
<td>0.4</td>
</tr>
<tr>
<td>MH</td>
<td>48 [10.2]</td>
<td>43.9 [13.5]</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Proportion of patients with postoperative low Physical or Mental QoL scores
Individual objective components of health, such as VO2max, when they are extrapolated from the patients contextual framework, may constitute only the basis of self-rating, which can be subsequently modified by the context of the evaluation.
CPET in the guidelines
Recommendations:

1- Cardio-pulmonary exercise tests are performed in controlled environment, reproducible and safe. Peak VO2 measured during an incremental exercise on treadmill or cycle should be regarded as the most important parameter to consider, as a measure of exercise capacity and highly predictive of postoperative complications.

*Level of evidence 2++; Grade of recommendations B*

2- The following basic cut-off values for peak VO2 should be considered:

- Peak VO2 > 75% of predicted value or 20 mL/min/kg qualifies for pneumonectomy
- Peak VO2 < 35% or 10 mL/min/kg indicates high risk for any resection.

Evidence is thin to recommend cut-off values for lobectomy

*Level of evidence 2++; Grade of recommendations C*
3.2.1.3. In patients with lung cancer being considered for surgery, with either a PPO FEV₁ < 30% predicted or a PPO DLCO < 30% predicted performance of a formal cardiopulmonary exercise test (CPET) with measurement of maximal oxygen consumption (\(\dot{V}O_2\)max) is recommended (Grade 1B).

3.9.2. In patients with lung cancer being considered for surgery and a \(\dot{V}O_2\)max < 10ml/kg/min or < 35% predicted it is recommended that they are counseled about minimally invasive surgery, sublobar resections or nonoperative treatment options for their lung cancer (Grade 1C).
Physiologic Evaluation of the Patient With Lung Cancer Being Considered for Resectonal Surgery

Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Algorithm for Thoracotomy and Major Anatomic Resection (Lobectomy or greater)

Positive high-risk cardiac evaluation

- VO2max <10 ml/kg/min Or < 35%

- VO2max 10-20 ml/kg/min Or 35%-75%

- VO2max >20 ml/kg/min Or >75%

Positive low-risk or Negative cardiac evaluation

- ppoFEV1 or ppoDLCO <30%

- ppoFEV1 or ppoDLCO < 60% AND both >30%

- ppoFEV1 and ppoDLCO > 60%

Actual Risks affected by parameters defined here and:
- Patient Factors: Comorbidities, age
- Structural Aspects: center (volume, specialization)
- Process factors: Management of complications
- Surgical access: Thoracotomy vs. minimally invasive
CPET and VATS lobectomy: is VO2max still a reliable indicator?
Mortality in High Risk patients

\[ \text{ppoFEV1 <40%} \]
- Open: 4.8%
- VATS: 0.7%
- \( p = 0.003 \)

\[ \text{ppoDLCO <40%} \]
- Open: 5.2%
- VATS: 2.0%
- \( P = 0.003 \)

Burt BM et al. JTCVS 2014; 148:19-28
1684 lobectomies patients with VO2max available in ESTS database
281 VATS lobectomies

Low VO2max (<15 ml/kg/min) was not associated with increased surgical risk after VATS lobectomy, challenging the traditional operability criteria