Cardiopulmonary Exercise Testing

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A 33-year-old man with a history of intermittent asthma presented with 3 months of dyspnea on exertion, which developed approximately 2 weeks after infection with SARS-CoV-2. His acute COVID-19 symptoms resolved after 5 days and did not require hospitalization. At presentation, his physical examination findings were normal and peripheral oxygen saturation was 97% at rest. Laboratory testing, chest radiographic imaging, chest computed tomographic scan, echocardiography, and pulmonary function testing results were normal. To further evaluate his dyspnea on exertion, the patient underwent cardiopulmonary exercise testing (CPET) on a cycle ergometer with arterial blood gas samples obtained from an indwelling radial artery catheter. Continuous 12-lead electrocardiogram (ECG) findings showed no evidence of arrhythmia or ischemia, and the patient stopped exercise due to leg fatigue after 15 minutes. Select exercise data are presented in the Table and Figure.

Table. Patient’s Select Cardiopulmonary Exercise Testing (CPET) Results

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Predicted</th>
<th>Measured</th>
<th>Percent predicted, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO₂max L/min</td>
<td>3.31</td>
<td>2.1</td>
<td>64</td>
</tr>
<tr>
<td>Maximum heart rate/min</td>
<td>187</td>
<td>164</td>
<td>88</td>
</tr>
<tr>
<td>Maximum oxygen pulseb</td>
<td>18</td>
<td>13</td>
<td>72</td>
</tr>
<tr>
<td>Anaerobic threshold, L/minc</td>
<td>1.32</td>
<td>0.85</td>
<td>25</td>
</tr>
<tr>
<td>Maximum blood pressure, mm Hg</td>
<td>170/86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum minute ventilation, L/min²</td>
<td>89</td>
<td></td>
<td></td>
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<tr>
<td>Exercise breathing reserve, L/min²</td>
<td>&gt;15</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>V̇E/V̇CO₂ at anaerobic threshold</td>
<td>&lt;34</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Pao₂ at maximum exercise, mm Hg</td>
<td>83.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paco₂ at maximum exercise, mm Hg</td>
<td>29.6</td>
<td></td>
<td></td>
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<tr>
<td>Arterial pH at maximum exercise</td>
<td>7.37</td>
<td></td>
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</tbody>
</table>

Abbreviations: Pao₂, arterial oxygen content; V̇E/V̇CO₂, minute ventilation/carbon dioxide production; VO₂max, maximum rate of oxygen consumption.

A. Predicted values were derived from Clinical Exercise Testing, 4th Edition.¹
B. VO₂ divided by heart rate at maximum exercise.
C. Respiratory rate multiplied by tidal volume at maximum exercise.
D. Maximum voluntary ventilation minus maximal ventilation at maximum exercise.

Answer
B. Cardiovascular limitation to exercise

Test Characteristics
CPET is a specialized type of exercise stress test performed on a stationary bicycle or treadmill during which progressively increasing resistance is applied until an individual is unable to continue exercising. During CPET, continuous ECG, continuous pulse oximetry, blood pressure monitoring, breath-by-breath measurement of oxygen and carbon dioxide, and arterial blood gas measurements are used to evaluate an individual’s cardiovascular, respiratory, and skeletal muscle responses to exercise.¹ CPET demonstrates whether an individual has decreased exercise capacity and can provide information about the cause(s) of exercise intolerance that are not identified by previous testing performed at rest.²³ The maximum rate of oxygen consumption (VO₂max) is determined by the efficiency of skeletal muscle, cardiovascular, and respiratory systems. A VO₂max that is lower than predicted for an individual's age and sex indicates reduced exercise capacity.

During CPET, the respiratory response to maximal exercise can be determined by an individual’s minute ventilation (respiratory rate times tidal volume), ventilatory efficiency (minute ventilation/carbon dioxide production), exercise breathing reserve, continuous pulse oximetry, and arterial blood gas analysis. The cardiovascular response to maximum exercise is assessed by ECG, heart rate, systolic and diastolic blood pressure, and oxygen pulse. The oxygen pulse, defined as the ratio of VO₂ to heart rate, provides an indirect estimate of stroke volume and typically increases with increasing workload.¹²³ Typical Medicare reimbursement for CPET in the US in 2021 was approximately $260.

Application of Test Result to This Patient
During CPET, this patient demonstrated reduced exercise tolerance, achieving only 64% of predicted VO₂max (Table and Figure, A). He had no evidence of a ventilatory limitation to exercise, based on his normal ventilatory efficiency, normal exercise breathing reserve, no desaturation on continuous pulse oximetry, and no hypoxemia on arterial blood gas at maximum exercise.²³ However, his CPET results demonstrated a cardiovascular limitation to exercise, shown by his low anaerobic threshold, the point at which lactic acid starts to accumulate in muscles due to anaerobic metabolism, along with a reduced maximum oxygen

HOW DO YOU INTERPRET THESE TEST RESULTS?
A. Cardiovascular and ventilatory limitation to exercise
B. Cardiovascular limitation to exercise
C. No limitation to exercise
D. Ventilatory limitation to exercise

Quiz at jamacmelookup.com
pulse and flattened oxygen pulse curve (Table and Figure, B). Although a low oxygen pulse and flattened oxygen pulse curve are typically caused by heart failure or myocardial ischemia, continuous ECG monitoring during CPET did not reveal evidence of myocardial ischemia and the patient’s recent echocardiogram showed normal biventricular function. Therefore, his cardiovascular limitation to exercise may have resulted from preload insufficiency due to low venous pressure associated with dysautonomia or from decreased peripheral muscle oxygen extraction due to mitochondrial or microvascular abnormalities.

A study of 10 patients with recent COVID-19 infection and no history of cardiopulmonary disease identified a marked reduction in VO₂max during CPET primarily due to a reduced systemic oxygen extraction. Treatment of patients with dyspnea after COVID-19 due to impaired extraction of oxygen involves implementation of a gradual, paced exercise regimen.

**What Are Alternative Diagnostic Testing Approaches?**

Invasive CPET involves insertion of a catheter in the pulmonary artery and radial artery to provide direct hemodynamic and blood gas analysis during CPET, which can help differentiate decreased peripheral extraction of oxygen from impaired oxygen delivery.

**Patient Outcome**

Based on CPET findings, the patient demonstrated a cardiovascular limitation to exercise, either due to preload insufficiency or decreased peripheral muscle oxygen extraction. A gradual reintroduction of exercise with a heart rate target of 125 beats/min to 130 beats/min was recommended. The patient adhered to this exercise plan and, 4 months after CPET, reported only mild residual intermittent dyspnea on exertion.

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**Clinical Bottom Line**

- Cardiopulmonary exercise testing (CPET) determines whether an individual has a limitation to exercise based on achieved maximum rate of oxygen consumption, VO₂max.
- CPET can identify the cause(s) of dyspnea on exertion that remain unexplained by testing performed at rest.
- Reduced exercise tolerance after COVID-19 infection has been reported, with individuals demonstrating a cardiovascular limitation on CPET despite normal echocardiography and electrocardiogram findings.

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**REFERENCES**