Cardiopulmonary exercise testing in the assessment of exertional dyspnea

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Abstract:
Dyspnea on exertion is a commonly encountered problem in clinical practice. It is usually investigated by resting tests such as pulmonary function tests and echocardiogram, which may at times can be non-diagnostic. Cardiopulmonary exercise testing (CPET) measures physiologic parameters during exercise which can enable accurate identification of the cause of dyspnea. Though CPET has been around for decades and provides valuable and pertinent physiologic information on the integrated cardiopulmonary responses to exercise, it remains underutilized. The objective of this review is to provide a comprehensible overview of the underlying principles of exercise physiology, indications and contraindications of CPET, methodology and interpretative strategies involved and thereby increase the understanding of the insights that can be gained from the use of CPET.

Key words: Anaerobic threshold, cardiopulmonary exercise test, carbon dioxide output, dyspnea, exercise limitation, oxygen uptake

Rationale for exercise testing
Exertional dyspnea is a common problem in patients with chronic lung diseases. This often leads to respiratory assessments such as spirometry, lung volume assessments, diffusing capacity, arterial blood gas determination, or cardiac assessments such as echocardiography. In essence, information from these tests which are performed in a resting state is used to assess a symptom which occurs with exertion. While this is often useful, exertional symptoms may correlate poorly with resting measurements.[1] Performing physiologic and subjective measurements during exercise often provides more relevant physiologic information and may give a more accurate estimate of functional capacity than testing done at rest in the laboratory. Furthermore, disease is often not confined to one organ system such as the lung, and testing the body’s overall physiological response to exercise will provide useful data. This provides the general rationale for exercise testing in the evaluation of exertional dyspnea.

Categories of exercise testing
Several types of exercise tests are commonly performed in the clinical assessment of patients. These can be divided into field and laboratory tests. The former include the timed walk test (e.g., the 6 minute walk test)[2] and the incremental and endurance shuttle walk tests.[3] Besides giving an overall measurement of exercise capacity, these are easy to perform, are related to daily functional activities, and may even predict morbidity or mortality. They do not, however, provide much physiologic information on exercise limitation. Laboratory tests of exercise performance include the incremental and constant work rate cardiopulmonary exercise tests (CPET). Both provide a wealth of physiologic data. Incremental testing provides information on maximal responses and anaerobic threshold. Constant work rate testing, usually performed at a high fraction of maximal work rate is commonly performed before and after an intervention, such as bronchodilator therapy or exercise training.

Cardiopulmonary exercise testing (CPET)
CPET provides a comprehensive assessment of the exercise response, and reflects the influences (including interactions) of the cardiac, respiratory, musculoskeletal and hematological systems.[4] This testing provides data on respiratory gas exchange, including oxygen uptake (V\text{O}_2), and carbon dioxide output (V\text{CO}_2), tidal volume (VT) and minute ventilation (V\text{E}), and other variables such as electrocardiographic, blood pressure and oxygen saturation. Testing can be done incrementally or at a constant work rate.

Integration of physiologic information allows for an analysis of the system as a whole,[5] while separate analyses help determine which system(s) limit exercise capacity or are related to exertional dyspnea. In general, CPET enables accurate determination of the physiologic reserves of the heart and lungs as well as functional capacity. Table 1 lists many of the physiologic variables measured during CPET.

Though CPET has been around for decades and provides valuable and pertinent physiologic information on the integrated cardiopulmonary responses to exercise, it remains underutilized. The
A brief review of exercise physiology

A working knowledge of exercise physiology is essential to understand the various aspects of CPET. This is schematically illustrated in Figure 1. During exercise, to provide the energy required by the muscles, oxygen (O₂) is inhaled into the lungs, transported by the pulmonary vessels to the heart and delivered to the muscles by the arterial circulatory system. Qₐᵲ is the O₂ utilized by the muscles and Q₉CO₂ is the carbon dioxide (CO₂) produced by muscles with exercise which is then transported by the venous system to the heart and lungs and then exhaled. Analysis of the measured inspired and expired gases during exercise enables quantification of the oxygen consumed or oxygen uptake (VO₂) and the CO₂ generated (VCO₂). In steady state, Q₀₂ = V₀₂ and Q₀CO₂ = VCO₂.

Table 1: Parameters measured during CPET

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
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<tr>
<td>Tidal Volume: VT</td>
<td>Breathing frequency: Respiratory Rate (RR or f)</td>
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<tr>
<td></td>
<td>Minute Ventilation: Vₜ = VT × RR</td>
</tr>
<tr>
<td>Rate of O₂ consumption: O₂ uptake (VCO₂)</td>
<td>Maximal VₐO₂ / VₐO₂ max</td>
</tr>
<tr>
<td>Rate of CO₂ elimination: CO₂ output (VCO₂)</td>
<td>Anaerobic threshold: AT</td>
</tr>
<tr>
<td>Respiratory Exchange ratio/Respiratory Quotient (RER/RQ)</td>
<td>Heart Rate Reserve (HRR)</td>
</tr>
<tr>
<td>HR vs. V₀₂ slope</td>
<td>O₂ pulse (V₀₂/HR)</td>
</tr>
<tr>
<td>Ventilatory Reserve (VR)</td>
<td>Ventilatory Equivalents for O₂ and CO₂ (Vₜ/V₀₂ and Vₜ/VCO₂)</td>
</tr>
<tr>
<td>Maximal ventilation (Vₚₚₚₚ)</td>
<td>End-tidal O₂: PETO</td>
</tr>
<tr>
<td></td>
<td>End-tidal CO₂: PETCO₂</td>
</tr>
<tr>
<td>Dead space/Tidal volume: V₀ₐ / Vₜ</td>
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</table>

Increased O₂ utilization by the muscles is achieved by increased O₂ extraction from blood perfusing exercising muscles, increased O₂ delivery by dilatation of the arteries, increased cardiac output (by increasing stroke volume and heart rate) and increasing pulmonary blood flow by recruitment of the pulmonary vasculature. As exercise results in increased CO₂ production, it is exhaled by the lungs by an increase in ventilation by a rise in tidal volume (VT) and respiratory rate.

Energy required for exercise is derived from adenosine triphosphate (ATP) which is generated in the cells by 3 processes — aerobic oxidation of glycogen and fatty acids, anaerobic hydrolysis of phosphocreatinine and anaerobic metabolism of glycogen. This is illustrated in Figure 2. In the early phase of exercise, local stores of muscle phosphocreatinine provide energy. Aerobic glycogen and fatty acid metabolism provide the major source of ATP and constitutes the only source during moderate intensity exercise. During heavy or sustained exercise, aerobic metabolism is unable to meet the demand; consequently, anaerobic generation of ATP occurs.

With aerobic metabolism, V₀₂ and VCO₂ are generated in proportion to the amount of glycogen and fatty acid oxidized, with increase in V₀₂ normally being slightly greater than the increase in VCO₂. With anaerobic metabolism, lactic acid generated, is neutralized by bicarbonate (HCO₃⁻), resulting in increased CO₂ production. Hence V₀₂ rises more than VO₂ in anaerobic exercise. This further burdens the ventilatory system, which must eliminate this excess CO₂.

The effects of increasing exercise intensity on ventilatory and gas exchange parameters are depicted in Figure 3. As work rate increases, VO₂, VCO₂ and minute ventilation (Vₜ) increases linearly till anaerobic metabolism causes lactic acidosis. Once lactic acidosis develops, HCO₃⁻ buffers lactate and more CO₂ is generated (H⁺ + HCO₃⁻ → H₂CO₃ → H₂O + CO₂). Consequently, rise in VCO₂ is higher than rise in VO₂ as more CO₂ is produced from HCO₃⁻ buffering of lactic acid. Vₜ rises at the same rate and in proportion to rise in VCO₂. Hence, Vₜ/V₀₂ and PETCO₂ remain unchanged while PET₀₂ and Vₜ/V₀₂ increases. With continued exercise, with worsening lactic acidosis, ventilation increases markedly to compensate for exercise-induced metabolic acidosis. The rise in Vₜ is more than the rise in VCO₂. So Vₜ/V₀₂ increases while PETCO₂ falls.
With increasing work, the point at which anaerobic metabolism begins is referred to as anaerobic threshold (AT). At AT, \( V_{O2} \) does not decrease but \( V_{CO2} \) rises due to buffering of lactic acid generated by anaerobic metabolism. In incremental exercise testing, the AT is usually expressed as the \( V_{O2} \) at which this process begins. It can be measured directly by demonstrating an increase in lactate in arterial blood or indirectly through its effects on \( V_{O2} \) and \( V_{CO2} \). Lactate entering the system is buffered by \( HCO_3^- \), resulting in an increase in the slope of \( V_{CO2} \) and resulting in increased VE. The indirect measurement of AT is commonly performed using the V-slope method [Figure 4], which determines when the \( V_{CO2} - V_{O2} \) slope abruptly increases.

During exercise, heart rate, respiratory rate, VT and \( V_e \) increase. \( V_{O2} \) and \( V_{CO2} \) rise steadily till anaerobic threshold is reached. With exercise, dead space (Vd) decreases due to increased pulmonary blood flow causing increased recruitment of pulmonary vessels. With increasing workload, \( V_{O2} \) peaks and remains constant, even though work intensity continues to increase. Maximal \( V_{O2} \) during exercise, which plateau and remains constant, despite further increases in exercise intensity is \( V_{O2\text{max}} \). It serves as an indicator of exercise capacity.

**Indications for CPET**

CPET is useful in determining the cause of exercise intolerance not diagnosed by history, physical examination, chest radiograph, PFTS and resting electrocardiogram and ECHO. Common indications for CPET are shown in Table 2. Absolute contraindications for CPET are shown in Table 3. Relative contraindications for CPET include uncontrolled hypertension (SBP > 200, DBP > 120), moderate cardiac valvular stenosis, hypertrophic obstructive cardiomyopathy, high-grade AV block, significant pulmonary hypertension, advanced/complicated pregnancy, significant dyselectrolytemia and orthopedic or neurologic impediments to exercise.

**CPET Methodology**

**Cycle ergometer or treadmill?**

Exercise testing in CPET is usually performed in the laboratory using a stationary cycle ergometer or a treadmill, although newer portable metabolic devices may permit exercise testing in non-traditional laboratory settings such as during activities of daily living. Whether a cycle ergometer or a treadmill is used often depends more on the equipment in the particular laboratory and experience and preference of the testers than the specific clinical indication of the testing. Exercise testing on a cycle ergometer is less likely to be associated with falls. Many consider the electrically braked cycle ergometry the preferred method of testing since it produces less movement artifact, facilitates obtaining arterial blood specimen drawing, provides a smooth increase in load. In addition, it is less affected by weight and gait dynamics which allows for a more accurate estimate of the externally applied work. An important advantage of treadmill testing is that, unlike cycling, walking and running are familiar activities that are incorporated into many activities of daily living.

**Table 2: Indications for CPET**

<table>
<thead>
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<th>Indication</th>
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<tr>
<td>Evaluation of dyspnea of unclear etiology after routine cardiopulmonary testing</td>
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<td>Determination of functional impairment in exercise intolerance</td>
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<tr>
<td>Evaluation of patients with heart disease for cardiac transplantation</td>
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<tr>
<td>Evaluation of patients for lung/heart-lung transplantation</td>
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<tr>
<td>Evaluation for exercise-induced bronchospasm</td>
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<tr>
<td>Preoperative evaluation prior to lung resection surgery</td>
</tr>
<tr>
<td>Assessment of response to therapeutic interventions in patients with lung disease</td>
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<tr>
<td>Evaluation for disability</td>
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<tr>
<td>Exercise prescription for cardiac and pulmonary rehabilitation</td>
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</tbody>
</table>

![Figure 4: The V-slope method of determining Anaerobic Threshold (AT)](http://www.thoracicmedicine.org)
daily living. \( V_{\text{O2max}} \) in treadmill exercise testing is considerably more affected by body weight with treadmill testing than cycle ergometry.\(^{[11,12]}\) Even if workload is estimated using weight, incline and speed, if the patient leans on the handrails this will introduce substantial error in this measurement.

Peak work rate, as expressed by \( V_{\text{O2}} \), is about 5-10% higher with treadmill testing than cycle ergometry\(^{[13]}\) probably because more muscles are used. Exercise-induced hypoxemia in COPD patients appears to be more pronounced during treadmill testing than on the cycle ergometer.

Exercise protocols
Most CPET protocols generally fall into two broad categories: 1. Incremental tests up to maximal exercise and 2. Constant work rate test.

These approaches provide different information and have different clinical indications. Incremental exercise testing involves gradually increasing work rate in a continuous or stepwise fashion over time. In cycle ergometer testing, work rate is usually increased by 5-25 watts each minute after a warm-up period of 1-3 minutes of unloaded pedaling. Exercise is usually continued to the point of symptom-limitation unless medical complications (such as chest pain, ECG changes, hemodynamic abnormalities, gait issues) develop. Criteria for terminating CPET\(^{[11]}\) include:

1. Chest pain suggestive of angina,
2. Ischemic EKG changes,
3. Complex ectopy or 2nd or 3rd degree AV block,
4. Drop in SBP > 20 mmHg from highest value during test,
5. Uncontrolled hypertension (SBP > 250 mmHg; DBP > 120 mmHg),
6. \( O_2 \) desaturation with \( O_2 \) saturation <80% or cyanosis and (viii) Dizziness or mental confusion or loss of coordination.

The pre-set rate increase in watts is determined by the exercise physiologist based on the physical state of the patient. In general, a test lasting 8-12 minutes is ideal.\(^{[14]}\) This is long enough to provide useful physiologic information yet not so long as to be burdensome to the patient and staff. In severely limited patients, 5 minutes exercise time is reasonable. Incremental treadmill testing is similar in concept, but requires gradual increase in walking speed and incline. Incremental testing provides information on maximal exercise performance (such as peak \( V_{\text{O2}} \)) and potential mechanisms limiting that performance.

A typical protocol for constant work rate cycle ergometer testing is to begin with a 1 to 3 minute period of unloaded pedaling for warm-up, then increase workload abruptly to a high percentage (such as 75%) of that patient’s maximal work rate.\(^{[11,13]}\) Exercise is generally continued to a symptom-limited maximum. This approach, therefore, requires a prior incremental test to determine maximal work rate and a period of time (usually one or more days) to recover from the first test. The constant work test is useful for determining response to therapeutic interventions such as bronchodilators and pulmonary rehabilitation.

Measurements
As stated earlier, an important advantage of CPET is that it not only determines maximal exercise performance, but also supplies important physiologic information during exercise. This may permit an analysis of physiologic derangement leading to exercise limitation and symptom-generation. The instruments used for measurement of physiologic variables during CPET are shown schematically in Figure 5.\(^{[11]}\) Stringent calibration of sensors to minimize errors is extremely important for quality control.

The primary physiologic measurements during CPET include the following physiologic information:

1. Cardiac monitoring: Continuous heart rate, rhythm, and ECG changes
2. Hemodynamic monitoring: Blood pressure at set intervals
3. Breath-by-breath analysis of inspired and expired gas: \( V_{\text{O2}}, V_{\text{CO2}} \)
4. Pneumotachograph: Tidal volume, respiratory rate, \( V_{\text{ IC}} \), inspiratory capacity (IC)
5. Pulse oximetry: Continuous measurement of oxygen saturation
6. Symptom assessment: Periodic assessments of dyspnea and leg fatigue using a category (Borg) or analog (visual analog) scale.

In selected cases, arterial blood is obtained during exercise testing to provide additional physiologic data. This may include:

1. Arterial blood gas determinations
2. Lactate levels

### Table 3: Absolute contraindications for CPET

<table>
<thead>
<tr>
<th>Condition</th>
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<tr>
<td>Acute coronary insufficiency</td>
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<tr>
<td>Syncope</td>
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<tr>
<td>Uncontrolled arrhythmia</td>
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<tr>
<td>Acute myocarditis/pericarditis</td>
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<tr>
<td>Decompensated heart failure</td>
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<tr>
<td>Acute pulmonary edema</td>
</tr>
<tr>
<td>Severe cardiac valvular stenosis</td>
</tr>
<tr>
<td>Suspected dissected aneurysm</td>
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<tr>
<td>Resting ( O_2 ) saturation &lt;85%</td>
</tr>
<tr>
<td>Acute Renal failure</td>
</tr>
<tr>
<td>Untreated thyrotoxicosis</td>
</tr>
<tr>
<td>Acute infection</td>
</tr>
<tr>
<td>Mental impairment/inability to follow instructions</td>
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</tbody>
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**Figure 5**: Automated system for CPET

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Physiologic parameters derived from the above measured data also provide important information. These derived measurements include: Ve/VO₂, Ve/VCO₂, VO₂max, O₂ pulse (VO₂/HR), Work efficiency (6 VO₂/6 WR), Anaerobic threshold (AT), Respiratory quotient (R) (VCO₂/VO₂), Dead space; (VD/VT), P (A-a) O₂, Heart Rate Reserve and Breathing Reserve.

In addition to numeric data, composite graphic display of ventilatory and gas exchange parameters can be generated.[16] Computer analysis of physiologic data allows the generation of VO₂ and VCO₂ on a breath-by-breath basis.[17]

Physiologic variables measured during CPET
The following parameters are important in the interpretation of CPET and are discussed in more detail.

Oxygen uptake (V̇O₂)[2,3,14]
This is calculated from the difference between the volume of O₂ in the inhaled and exhaled air during exercise per unit of time and in steady state is equal to metabolic O₂ consumption. The measurement of V̇O₂ is based on the equation:

\[ V̇O₂ = VI \times FIO₂ - VE \times FEO₂ \]

where VI = Volume of inhaled air
VE = Volume of exhaled air
FIO₂ = Concentration of O₂ in the inhaled gases
FEO₂ = Concentration of O₂ in the exhaled gases

V̇O₂ is determined by cellular O₂ demand and increases linearly as external work increases. In healthy subjects, a faster rate of increase in work results in a greater amount of work being achieved while peak VO₂ achieved is independent of the rate of increase in work.[19] The slope of the relationship between the increase in work versus the change in VO₂ determined during incremental CPET is unaffected by age, sex or height. A reduction in the value of this relationship is indicative of the abnormalities in O₂2 transport and utilization.

As work increases, V̇O₂ increases until a point where it begins to plateau. This represents the highest attainable V̇O₂ for a subject and is known as maximal V̇O₂ or V̇O₂max. It represents the maximal achievable level of oxidative metabolism involving large muscle groups. If a clear plateau is not obtained during CPET, the highest VO₂ attained is the V̇O₂peak and can be used as a substitute for V̇O₂max. V̇O₂max (as well as V̇CO₂max) serves as the index of aerobic exercise capacity. V̇O₂max and V̇CO₂max should be expressed as an absolute value (in Liters/minute) as well as a percentage of predicted, referenced to body weight (in milliliters/kg/minute). A reduced V̇O₂max or V̇CO₂max reflects reduced exercise capacity which may be due to cardiac, pulmonary, gas exchange, neuromuscular, muscular or effort limitation. However, in obesity, VO₂max and V̇CO₂max are reduced in reference to body weight but the absolute value remains normal.[29]

Carbon dioxide output (V̇CO₂)
This is calculated from the difference between the volume of CO₂ in the inhaled and exhaled air during exercise per unit of time and represents metabolic CO₂ output. The measurement of V̇CO₂ is based on the equation:

\[ V̇CO₂ = VE \times ḞCO₂ \]

where VE = Volume of exhaled air
ḞCO₂ = Concentration of CO₂ in the exhaled gases

V̇CO₂ is affected by the same factors as V̇O₂. However, it is more dependent on ventilation due to the increased solubility of CO₂ in the blood. Several variables in CPET including the RER/ RQ, V̇O₂/V̇E, and ventilatory equivalents are derived from V̇CO₂.

Respiratory exchange ratio (RER)
This is derived from the ratio of V̇CO₂/V̇O₂ and corresponds to the gas exchange ratio. In steady state, it equals the Respiratory Quotient (RQ) which represents metabolism at the tissue level. Metabolism predominantly from carbohydrates results in an RQ of 1, while metabolism of protein results in an RQ of 0.8 and from fat, an RQ of 0.7. The production of lactic acid during exercise results in an RER greater than 1, since extra CO₂ is introduced into the system from bicarbonate buffering of the acid. Therefore an RER substantially greater than 1 at peak exercise is one marker of maximal effort. Hyperventilation may also cause an RER>1.

Anaerobic threshold (AT)
This represents the VO₂ at which anaerobic metabolism sets in during exercise. It can be expressed in L/min or as a percentage of the predicted value of V̇O₂max. Direct measurement of AT requires continuous arterial sampling of lactate. However, it can be reasonably estimated from continuous physiologic data. In the modified V-slope method the AT is identified as that point where the slope of the relationship of V̇CO₂ to V̇O₂ changes. The abrupt increase in VCO₂ indicates an increase in the rate of CO₂ production from lactate buffering by bicarbonate.[21] In many cases the AT cannot be estimated from physiologic data. In other cases, exercise is limited before the AT is reached, such as in ventilatory-limited COPD patients. Its normal value is >40% of predicted V̇O₂max.

Heart rate reserve (HRR)
It is the difference between maximum predicted heart rate and the observed maximum heart rate during CPET. Its normal value is <15. A high HRR may indicate a sub-maximal effort.

V̇O₂-work rate relationship
The relationship between VO₂ and work rate at peak work rate is approximately 10 mL/min/watt. Values lower than this suggests abnormalities with oxygen delivery. It may be elevated in obesity.

O₂ pulse (V̇O₂/HR)
This is determined by dividing VO₂ by HR and is expressed as mL/beat. A low O₂ pulse during exercise may indicate a reduced stroke volume or an abnormality in skeletal muscle O₂ extraction. A low HR during exercise, such as from beta-blocker medications, may elevate the O₂ pulse by decreasing the denominator.

Maximal ventilation (V̇Emax)
Minute ventilation (V̇E) is the volume of air exhaled from the lungs in 1 min. With exercise, V̇E increases due to increase in both tidal volume and respiratory frequency. The normal maximal value of respiratory frequency is less than 60 breaths per minute while the maximal VT is generally less than 60% of the vital capacity.[22] V̇Emax is the maximal ventilation achieved during exercise, reflects ventilatory demand.[23] Abnormalities
in $V_{Emax}$ may indicate respiratory or neuromuscular limitation to exercise.

**Ventilatory reserve (VR)**

This reflects the difference between the measured or estimated maximal voluntary ventilation (MVV) and the $V_{Emax}$. MVV is the volume of air that can be breathed per minute at rest with maximal effort. While the MVV can be determined in the lab, it can be reasonably estimated by multiplying the FEV1 by 35. VR is usually determined by the formula: $VR = \left( \frac{V_{Emax}}{MVV} \right) \times 100$. Normal values are $\geq 15\%$ to $\leq 85\%$. VR is usually reduced in individuals with ventilatory limitation to exercise, such as patients with obstructive airways disease or interstitial lung disease.

**Ventilatory equivalents for O$_2$ and CO$_2$ ($V_E/V_O2$ and $V_E/V_CO2$)**

The ventilatory equivalent for O$_2$ ($V_E/V_O2$) is the ratio of $V_E$ to $V_O2$ while the ventilatory equivalent for CO$_2$ ($V_E/V_CO2$) is the ratio of $V_E$ to $V_CO2$. With increasing exercise, $V_E/V_O2$ initially falls, reaches its nadir near the anaerobic threshold, and then rises. $V_E/V_CO2$ follows a similar trajectory, but rises after the rise in $V_E/V_O2$ due to compensatory hyperventilation to counter metabolic acidosis. High values of $V_E/V_CO2$ are indicative of increased dead space during exercise. If the $V_E/V_O2$ and $V_E/V_CO2$ do not rise with maximal exercise that indicates high airway resistance or a general increase in pulmonary muscle load. Both increase with hyperventilation.

**Dead space to tidal volume ratio ($V_D/V_T$)**

The $V_D/V_T$ reflects the adequacy or efficiency of gas exchange. With exercise, $V_D/V_T$ decreases as tidal volume increase in response to increased metabolic demand and dead space ventilation remains relatively unchanged. An elevated $V_D/V_T$ or absence of reduction in $V_D/V_T$ with exercise suggests pulmonary vascular disease such as pulmonary hypertension.

**Interpreting data from CPET**

Exercise limitation during CPET is indicated by a reduced VO$_2$ peak. Exercise limitation could be secondary to cardiovascular, ventilatory, gas exchange, or neuromuscular limitation. In addition, physical deconditioning and poor effort are also considerations. Moreover, exercise limitation may result from several of the above limitations, although one factor is usually of more significance than the others. Furthermore, overlap in response patterns to exercise may exist, sometimes making exact distinctions in mechanisms of exercise limitation problematical.

Before interpreting a CPET, it is essential to assess whether patient effort was adequate. Adequate effort is indicated by the following:
1. Attaining maximal predicted heart rate,
2. Attaining maximal predicted minute ventilation ($V_E$),
3. RQ $> 1.15$, (iv) patient showing signs of exhaustion.
Other conditions, such as significant $\text{O}_2$-desaturation, chest pain, lightheadedness, ECG abnormalities, orthopedic symptoms, or unexpected changes in blood pressure, may limit exercise before maximal effort is attained.

Certain physiologic patterns during exercise may indicate the cause of exercise limitation. The CPET pattern in some common disease states causing exercise limitation is as follows:

**CPET pattern in cardiac disease**

Exercise capacity is reduced as indicated by a reduced $\text{VO}_{2\text{max}}$. Cardiovascular responses are abnormal—heart rate reserve is decreased or absent and $\text{O}_2$ pulse is reduced. Anaerobic threshold (AT) is early onset and less than 40% predicted $\text{VO}_{2\text{max}}$. Ventilatory responses are normal, including normal Ventilatory Reserve ($V_{\text{Emax}}/\text{MVV}$), normal maximal respiratory rate (<50/minute) and a normal $\text{paCO}_2$. In cardiac disease, gas exchange may be mildly abnormal, with a mildly reduced dead space ($V_d/V_t$) at rest and a mildly increased ventilatory equivalents for $\text{O}_2$ and $\text{CO}_2$ ($V_e/\text{VO}_2$ and $V_e/\text{VCO}_2$) at AT.

The effect of exercise on physiologic parameters studied during CPET in a normal subject is shown in Figure 6. The changes in various physiologic parameters with exercise in heart disease (cardiac limitation to exercise) are depicted graphically in Figure 7.

**CPET pattern in lung disease**

Exercise capacity ($\text{VO}_{2\text{max}}$) is reduced. Ventilatory responses are abnormal: Maximal voluntary ventilation (MVV) and Ventilatory Reserve ($V_{\text{Emax}}/\text{MVV}$) are reduced; respiratory rate at maximal exercise is increased (>50/minute) and hypercapnia may be present. Cardiovascular responses are normal borderline abnormal. Heart rate reserve may be increased or normal; $\text{O}_2$
pulse will be normal and AT may be normal or indeterminate. Mild gas exchange abnormalities may be present such as increased dead space (\(V_d/V_t\)) at rest with < normal reduction with exercise and ventilatory equivalent for \(CO_2\) and \(O_2\) (\(V_e/\text{VCO}_2\) and \(V_e/V_{O2}\)) may be mildly increased with reduced \(pO_2\) or oxygen saturation with exercise. Individuals with ventilatory limitation to maximal exercise may have an increased heart rate reserve at peak exercise because ventilatory limitation may have occurred before cardiovascular limitation set in. The AT may be normal, reduced or indeterminate in individuals with ventilatory limitation. A decrease in end-tidal \(O_2\) (\(PETO2\)) and \(CO_2\) (\(PETCO2\)) also indicates ventilatory limitation. The changes in various physiologic parameters with exercise in lung disease (ventilatory limitation to exercise) are depicted graphically in Figure 8.

**CPET pattern in pulmonary vascular disease**

Exercise capacity is reduced, with a reduced \(V_{O2max}\). Cardiovascular responses are abnormal with low or absent heart rate reserve and low \(O_2\) pulse. AT is early onset and reduced to <40% of predicted \(V_{O2max}\). Gas exchange is significantly abnormal with a moderate-to-severely increased dead space-to-tidal volume ratio (\(V_d/V_t\)) at rest and no reduction in \(V_d/V_t\) with exercise. Ventilatory equivalent for \(O_2\) and \(CO_2\) (\(V_e/\text{VCO}_2\) and \(V_e/V_{O2}\)) at AT is markedly increased with a low \(pO_2\)/oxygen saturation and a markedly increased A-a gradient. In pulmonary vascular disease, ventilatory responses are normal with a low normal Ventilatory Reserve (\(V_{Emax}/\text{MVV}\)), respiratory rate at maximal exercise <50/minute and a normal \(p\text{aCO}_2\). The AT may or may not be reduced with gas exchange limitation. The changes in various physiologic parameters with exercise in pulmonary vascular disease (gas exchange limitation to exercise) are depicted graphically in Figure 9.\(^7\)

Otherwise healthy obese individuals have increased workload during exercise, but often their physiologic patterns are

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**Figure 8:** Graphic display of response to exercise in patient with heart disease on cardiopulmonary exercise testing (cardiac limitation to exercise)
normal. The peak VO\textsubscript{2} in obesity is normal when expressed as L/min, but is low when expressed as ml/kg/min.\textsuperscript{[25]} Exercise limitation due to physical deconditioning is characterized by reduced V\textsubscript{O2peak} or V\textsubscript{O2peak} as such it may be difficult at times to differentiate from disease state limitations. Heart rate reserve may be reduced or absent. AT may be normal or reduced; O\textsubscript{2} pulse is reduced.\textsuperscript{[4]} There is no evidence of ventilatory and gas exchange abnormalities. Suboptimal effort may be suspected by premature cessation of exercise, a reduced V\textsubscript{O2peak}, a normal or unattained AT, in conjunction with markedly increased heart rate reserve and ventilatory reserve and low RQ. The presence of irregular and erratic breathing patterns and respiratory rates unrelated to increase in work may be a clue to malingering.

**Conclusion**

The evaluation of exercise symptoms, such as exertional dyspnea, usually begins with tests done at rest, such as spirometry, echocardiography, or radiographic procedures. These assessments often provide useful information relating to the diagnosis of the limitation and its severity. CPET should be considered when there is some discord between the patient’s symptoms or stated level of exercise limitation and the baseline diagnostic information. It makes sense to assess symptoms, limitation and physiologic responses during exercise rather than inferring these responses from tests done at rest. CPET adds complementary information to our usual diagnostic testing. The information obtained from CPET can alter the management of an individual patient by identifying the cause of exercise limitation. In some cases, exertional dyspnea may be related to obesity and deconditioning, which can be detected by CPET and help to provide reassurance to patients, as well as prevent further utilization of resources in further testing to determine cause of exercise intolerance.

**References**


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