Cardiopulmonary Exercise Testing– Clinical Implications

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Outline

- Basic concepts
- Case studies
- Recent advances in clinical applications of CPET

Basic Concepts

Exercise

- Any physical activity in which work is performed by skeletal muscle can be regarded as exercise
- 2 types
  - Resistance exercise(brief periods of muscle contraction at high forces) eg weightlifting
  - Endurance/aerobic exercises (lower intensity contractions performed rhythmically for extended periods of time)eg. Walking, running and cycling

Cardiopulmonary exercise testing (CPET)

- Relatively noninvasive, dynamic physiologic test that permits the evaluation of both submaximal and peak exercise responses
- Provides a global assessment of the integrative exercise responses involving the pulmonary, cardiovascular, hematopoietic, neuropsychological, and skeletal muscle systems, which are not adequately reflected through the measurement of individual organ system function
- Provides the physician with relevant information for clinical decision making

Indications

- Evaluation of exercise tolerance
  - Determination of functional impairment or capacity (peak V˙ O2)
  - Determination of exercise-limiting factors and pathophysiologic mechanisms

- Evaluation of undiagnosed exercise intolerance
  - Assessing contribution of cardiac and pulmonary etiology in coexisting disease
  - Symptoms disproportionate to resting pulmonary and cardiac tests
  - Unexplained dyspnea when initial cardiopulmonary testing is nondiagnostic

Indications

- Evaluation of patients with cardiovascular disease
  - Functional evaluation and prognosis in patients with heart failure
  - Selection for cardiac transplantation
  - Exercise prescription and monitoring response to exercise training for cardiac rehabilitation (special circumstances; i.e., pacemakers)

Indications-Evaluation of patients with respiratory disease

- Chronic obstructive pulmonary disease
  - Establishing exercise limitation(s)
  - Assessing other potential contributing factors, especially occult heart disease (ischemia)
  - Determination of magnitude of hypoxemia and for O2 prescription
  - Objective determination of therapeutic intervention
- Interstitial lung diseases
  - Detection of early (occult) gas exchange abnormalities
  - Determination of potential exercise-limiting factors
  - Documentation of therapeutic response to potentially toxic therapy

Indications

- Pulmonary vascular disease (careful risk–benefit analysis required)
- Cystic fibrosis
- Exercise-induced bronchospasm

Specific clinical applications

- Preoperative evaluation
  - Lung resectional surgery
  - Elderly patients undergoing major abdominal surgery
  - Lung volume reduction surgery for emphysema
- Exercise evaluation and prescription for pulmonary rehabilitation
- Evaluation for impairment–disability
- Evaluation for lung, heart–lung transplantation

Contraindications

- Acute MI (in first week)
- Active endocarditis/pericarditis/myocarditis
- LMCA stenosis
- High degree heart block
- Pulmonary edema
- Respiratory failure
- Significant pulmonary hypertension

Indications for Exercise Termination

- Chest pain
- Ischemic ECG changes
- Heart block
- HTN SBP > 250 or DBP >120
- $SpO_2 < 80\%$
- Sudden pallor
- Faintness
- Respiratory failure

Equipment

- Exercise equipment
- Airflow or volume transducers
- Gas analysers
- Electrocardiograph
- NIBP
- Pulse oximetry
- Intraarterial BP monitoring and ABG (invasive, optional, SOS)

How we do it?

Exercise Protocol

- Maximal incremental cycle ergometry protocol
- Maximal incremental treadmill protocol
- Constant work rate protocol

Measurements during CPET

Measurements	Noninvasive	Invasive
External work	WR	
Metabolic gas exchange	VO2, VCO2, RER, AT	Lactate/ bicarbonate
Cardiovascular	HR, ECG, BP, Oxygen pulse	
Ventilatory	Ve, Vt, fR	
Pulmonary gas exchange	SpO2, Ve/VCO2, Ve/VO2, Pet O2, Pet CO2	pH, pCO2, pO2, SaO2, P(A-a) O2, Vd/Vt
Symptoms	Dyspnea, fatigue, chest pain	

Variables Used for Interpreting Results

V_{O2} max and Peak V_{O2}

- V_{O2} max
  - Represents maximal achievable oxidative metabolism using large muscle groups
  - Clear plateau achieved during exercise
  - Gold standard for cardiopulmonary fitness
- Peak V_{O2}
  - V_{O2} at maximal exercise without a plateau
  - Used interchangably with V_{O2} max

V_{O2} max

- Low V_{O2} max: Starting point in evaluation of reduced exercise tolerance
- Normal values
  - Men: [Ht (cm) – Age (yr)] X 21
  - Women: [Ht (cm) – Age (yr)] X 14
  - LLN: 83% of predicted
- Decreased in:
  - CHF, COAD, IPF, Pulmonary vascular disease (PVD), deconditioning, anemia

V_{O2}-Work Rate Relationship

- $\Delta V_{O2}/\Delta WR$ - Slope represents the efficiency of the metabolic conversion of chemical potential energy to mechanical work
- Independent of age, sex and height
- V_{O2} for a given WR is higher in obese but slope is normal
- Normal value: 10.0 ml/min/watt (LLN: 8.5)
- High in: obesity, hyperthyroidism, poor exercise technique

Respiratory Exchange Ratio (RER)

- Ratio of V_{CO2}/V_{O2}
- Under steady state: equals RQ (cellular level)
- At rest, < 1.0, near to 0.8 (mixed metab of carbohydrates, fats and proteins)
- During exercise, equals 1 (glycogen primarily metabolised)
- Exceeds 1, when anaerobic threshold is reached

Anaerobic Threshold (AT)

- Term *introduced by* Wasserman and McIlroy in 1964[1]
- Critical or threshold level of work above which exercise is associated with a systemic lactic acidosis, indicative of nonoxidative glycolysis
- Normal value: 50-60% of V_{O2}max (LLN: 40%)
- Marker of exercise that cannot be sustained for very long

[1]Wasserman K,et al. Am J Cardiol 1964; 14:844-852.

Anaerobic Threshold

- Non specific marker like V_{O2} max
- Decreased in:
  - Heart failure
  - Pulmonary vascular disease
- Can be decreased or normal in:
  - COAD
  - ILD
  - Deconditioning

Determination

- Invasive
  - Arterial lactate: by ABG every 2 min
  - Arterial bicarbonate: if lactate NA
- Noninvasive
  - Modified V-slope method -- Point of change in slope of relationship of V_{CO2} versus V_{O2} (V_{O2} above which V_{CO2} increases faster than V_{O2} without hyperventilation)

Heart rate

- Maximal predicted heart rate: 210 – (age X 0.65)
  - LLN: > 90% of predicted
- Heart rate reserve (HRR): Difference between age predicted maximal HR and actual heart rate achieved during exercise
- Normal: < 15 beats/min
- Maximal heart rate response decreased in multiple cardiorespiratory diseases

Blood Pressure Response

- Systolic BP progressively with increasing V_{O2}
- Diastolic BP remains constant or may decline slightly
- Abnormal responses: excessive rise, reduced rise or a fall
- Higher limit of normal: < 220/90

Oxygen Pulse

- Ratio of V_{O2} to HR
- Fick's equation: CO = SV X HR = VO2/ C (a-v) O2
- On rearranging:

  V_{O2}/HR (oxygen pulse) = SV X C (a-v) O2
- Increases with incremental exercise, till it flattens at maximal work rate
- Low flat oxygen pulse represents low stroke volume: heart failure, pulmonary vascular disease, deconditioning

Ventilation

- During exercise: both Vt and fR increase till 70-80% of peak exercise thereafter, fR predominates
- Vt plateaus at 50-60% of VC
- Ventilatory demand: Ve at a given level of exercise
- Increased in : COAD, ILD, PVD (due to increased dead space ventilation, V-Q mismatch, stimulation of lung receptors)

Ventilation

- Ventilatory capacity: maximal minute ventilation (MVV), best measure of ventilatory capacity till date
- MVV = FEV1 X 35-40
- Ventilatory Reserve: Reciprocal of
  - Ve peak/ MVV X 100
  - Normal: < 85% (72 ± 15%)
- Or alternatively, MVV – Ve peak (>11 L)

Ventilatory Reserve

- Good discriminatory value
- Ve peak/MVV high in COAD (reaches 100% or higher)
- High in ILD, but lower than COAD
- Normal or decreased in heart failure

V_E - V_{CO2} Relationship

- V_E/V_{CO2}: Represents ventilatory response in relation to rise in CO2 production
- Normal: < 34 (L/L) at AT
- Increased in COAD, ILD, heart failure, PVD
- Discriminates cardiopulmonary disorders from obesity and deconditioning

V_E - V_{CO2} Relationship

- Rise in V_E/V_{CO2} low if insensitivity to high PaCO2 and ventilatory restriction as in some COAD patients
- V_E/V_{CO2} high (with low P_{ET} CO2): hyperventilation (psychogenic: HVS/ anxiety)

Pulmonary Gas Exchange

- Significant hypoxemia:
  - SpO2 $\leq$ 88% or
  - PaO2 $\leq$ 55mmHg or
  - ΔSpO2 $\geq$ 4%
- Differentiates between predominantly cardiac and pulmonary cause
- More in ILD, PVD than in COAD
- P (A-a) O2: Increased in ILD, PVD and some COAD (Normal: <35)

Dead Space

- Physiologic dead space to tidal volume (Vd/Vt)
- Vd/Vt $(PaCO_2 - P_ECO_2)/PaCO_2$
- $P_E\ CO_2$ = mixed expired value of alveolar and dead space gas
- Normal: 0.28
- Increased in COAD, ILD, heart failure, PVD
- Discriminates cardiopulmonary disease from deconditioning and obesity associated limitation

Perceptual Assessment -- Symptoms

- Grading of dyspnea and leg muscle fatigue
  - VAS : 0 to 100 or
  - Borg's category ratio (CR-10) scale: 0 to 10 (open ended) along with verbal descriptors of severity
- Usually recorded at peak exercise
- Can be recorded at multiple time points during exercise
- Ratings of dyspnea and fatigue are reduced after pulmonary rehabilitation

Recent Advances in Clinical Applications of CPET

Evaluation of Exercise Capacity after Lung Transplantation

Lung Transplantation

- Bartels MN[1]
- 153 patients transplanted over 7 years who had complete cardiopulmonary exercise testing (CPET) and pulmonary function tests (PFT) pre- and post- lung transplantation
- Pulmonary function markedly improved post-transplant as forced vital capacity increased 67%, maximum voluntary ventilation increased 91% and forced expired volume in 1 second increased 136%.

[1] Chest 2011 Jun 16. [Epub ahead of print]

Bartels et al

- VO2 max increased only 19%, peak carbon dioxide production increased 50% and peak work increased 78%
- Although 1.5 to 2.0-fold increase in exercise capacity post- transplant, peak exercise capacity remained at 50% of the predicted normal, suggesting a maximal limitation
- Indicates poor strength, deconditioning or other peripheral factors play a significant role in the limitation of exercise benefit post-transplantation

Prognostication of Patients with ILD

Idiopathic Pulmonary Fibrosis

- Fell CD et al[1]
- 117 patients with IPF and longitudinal cardiopulmonary exercise tests were examined retrospectively
- Baseline maximal oxygen uptake less than 8.3 ml/kg/min had an increased risk of death (n = 8; hazard ratio, 3.24; 95% confidence interval, 1.10-9.56; P = 0.03) after adjusting for age, gender, smoking status, baseline forced vital capacity, and **baseline diffusion capacity for carbon monoxide**

[1] Am J Respir Crit Care Med. 2009 Mar 1;179(5):402-7

Evaluation of PR in COAD

Lan CC et al[1]

- Twenty-two underweight COPD patients who participated in 12-week, hospital-based outpatient PRP consisting of two sessions per week. Baseline and post-PRP status were evaluated by spirometry, cardiopulmonary exercise testing, ventilatory muscle strength and the St. George's Respiratory Questionnaire (SGRQ)
- Significant improvements in peak oxygen uptake, peak workload and the SGRQ total, symptoms, activity and impact scores in both underweight and non-underweight patients with COPD (all $P < 0.05$)

[1]Respirology 2011 Feb;16(2):276-83

Summary

- CPET is a dynamic physiologic test that permits the evaluation of both submaximal and peak exercise responses
- Major indications include evaluation of exercise intolerance in undiagnosed as well as known patients of cardiorespiratory diseases
- V_{O2} max and anaerobic threshold are two most important measures of exercise capacity

- CPET helps to differentiate cardiopulmonary causes of exercise limitation from peripheral and neuropsychological causes
- Helps to discriminate between cardiac and pulmonary contribution to a patient’s exercise intolerance