Physiological basis of preoperative cardiopulmonary exercise testing

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Abstract

The use of cardiopulmonary exercise testing (CPET) is gaining popularity as a preoperative functional assessment tool and a useful adjunct to risk stratification before surgery. Determination of the integrated response of multiple body systems (including the cardiorespiratory and peripheral oxygen delivery systems) to exercise stress, adds important prognostic value to pre-surgical assessment, shared-decision making and postoperative management of the surgical patient. Thorough CPET interpretation is complex but may be assisted by an understanding of basic exercise physiology and its application to the preoperative context.

Keywords Cardiopulmonary exercise testing; decision making; physiology; preoperative investigation

Introduction

The ability to carry out strenuous exercise or to survive the physiological stresses of major surgery depends largely on overall physical fitness. This fitness is the end product of the inter-related functioning of the cardiovascular and respiratory systems, along with intracellular metabolic capabilities.

Cardiopulmonary exercise testing (CPET) is becoming increasingly popular as a preoperative assessment tool. This is consistent with the increasing body of evidence supporting the importance of cardiorespiratory reserve as an independent predictor of perioperative morbidity and mortality following major surgery.[1−3] CPET has significant pedigree in the subjective assessment of disease severity and progression in heart failure[4−6] and other systemic illness.[7−9]

The American Thoracic Society and American College of Chest Physicians (ATS/ACCP) joint statement on CPET list the following indications for CPET:[10]

- evaluation of exercise tolerance
- evaluation of undiagnosed exercise intolerance
- evaluation of patients with cardiovascular disease
- evaluation of patients with respiratory disease/symptoms
- preoperative evaluation
- exercise evaluation and prescription for pulmonary rehabilitation
- evaluation of impairment/disability
- evaluation for lung, heart and heart−lung transplantation.

The benefit of CPET is the objective assessment of integrated multisystem function during exercise stress, with the ability to comment on cardiorespiratory reserve, disease diagnosis and reasons for exercise limitations. Competent analysis of the significant amount of data produced requires an understanding of the physiology of exercise and how it applies to the test.

What is a cardiopulmonary exercise test?

Preoperative CPET involves the continuous measurement of respiratory gases through a period of increasing resistance (ramped) exercise. During this period 12 lead electrocardiography (ECG), non-invasive blood pressure (BP) and oxygen saturation can also be measured. CPET is a reproducible, objective test that allows the assessment of cardiac, respiratory, vascular and muscular systems in the delivery and utilization of oxygen. Since exercise represents a physiological stressor, its value in the preoperative setting is through extrapolation to the stress promoted by major surgery.

Test delivery

All tests commence with attachment of monitoring equipment. This includes:

- face mask to measure breath-by-breath gas exchange,
- ECG
- blood pressure cuff
- oxygen saturation probe.

Application of exercise stress can be undertaken on a treadmill or by cycle ergometry. In clinical exercise practice, cycle ergometry is the method of choice. Most UK centres performing CPET for preoperative assessment conform to a standard protocol consisting of four continuous phases.

These four phases are as follows.

1. **Rest:** 2−5 minute period remaining stationary on the cycle. This allows for the patient to become accustomed to the equipment.
2. **Unloaded cycling (freewheel):** 3 minute period of cycling against no resistance, allowing stabilization of baseline measurements and avoiding any potential confounding factors such as anxiety-driven hyperventilation.
3. **Ramped exercise:** Continual, ramped resistance to pedalling. Protocols are designed to produce a maximum predicted work for an individual in approximately 10 minutes. The speed at which resistance is increased will depend on patient's age, sex and comorbidities. Resistance should be removed when the subject is unable to continue (symptom-limited exercise). Communication and encouragement should take place throughout.
4. **Recovery:** Pedalling against no resistance with continued monitoring of variables until heart rate returns within 10 bpm of pretest.

By plotting graphs with combinations of the haemodynamic and ventilatory variables measured, specific relationships can be identified as to the performance of multiple body systems,

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particularly the cardiovascular and respiratory systems. Various graphical demonstrations of the data may be presented. The commonest summary of the combined data is the nine panel plot characterized by Wasserman et al.[11]

Physiology of exercise testing

Oxygen transport during ramped exercise

In exercise testing, the physiological path of oxygen from atmosphere to muscle and the return journey through carbon dioxide can be assessed. This journey involves the oxygen cascade through respiratory, cardiovascular and peripheral vascular systems to skeletal muscle.

When considering oxygen, oxygen uptake (VO_2 in ml/min) can be shown as:

- $VO_2 = (SV \times HR) \times (CaO_2 - CvO_2)$ during exercise
- $VO_2max = (SVmax \times HRmax) \times (CaO_2max - CvO_2max)$ at maximal exercise

where SV is stroke volume, HR is heart rate, CaO_2 is arterial oxygen content and CvO_2 is central venous oxygen content.

During increasing resistance exercise, the body will increase oxygen delivery to its maximal ability in an attempt to maintain efficient energy production. This can be seen by an increase in minute volume ventilation and cardiac output as a consequence of increasing metabolic requirements.

Metabolism during ramped exercise

The increased metabolism caused by exercise stress during CPET requires utilization of energy resources. Aerobic metabolism is efficient in that each molecule of glucose, as a substrate for metabolism, produces 36–38 adenosine triphosphates (ATP) through the involvement of glycolysis, the tricarboxylic (TCA) cycle and the electron transport chain. Every oxygen molecule (O_2) used in this process produces an equivalent number of carbon dioxide (CO_2) molecules.

As exercise continues to increase, the continued production of ATP will begin to rely more on anaerobic metabolism as aerobic pathways approach their maximum function. Anaerobic metabolism is less efficient in terms of ATP production and creates an excess of H^+ ions, which are buffered by bicarbonate to produce H_2O and CO_2 governed by the following equation:

$$[H^+] + [HCO_3^-] <-> [H_2CO_3] <-> [CO_2] + [H_2O]$$

This excess production of CO_2, over and above that produced by ongoing aerobic metabolism, will alter the equivalence of O_2 utilization and CO_2 production. In terms of respiratory gases, the relationship between VO_2 and VCO_2 (where VO_2 is oxygen uptake and VCO_2 carbon dioxide production in ml/minute), will also change and the anaerobic threshold is defined as the VO_2 at which this change occurs.

Measurable outcomes of CPET test (Figure 1)

Peak and maximal oxygen uptake: if oxygen uptake is plotted against work, the VO_2 will increase in a linear fashion (in cycle ergometry approximately 10 ml/minute/watt). This will continue until the maximal level of work is reached as one of the system variables reaches its limit (e.g. stroke volume, heart rate or ventilation), representing the maximal achievable oxidative metabolism in large muscle groups. At this point the VO_2 will plateau representing VO_2 max. However, in the clinical setting, symptoms will more often limit the ability of an individual to continue, making the development of a plateau impossible. Therefore, the term VO_2 peak is often used which indicates the maximal value of VO_2 before stopping the test. This value represents the gold standard for cardiorespiratory fitness in the view of the ATS/ACCP.[10] It has also been shown to be an independent predictor of postoperative complications in intra-abdominal surgery.[3] However, maximal oxygen parameters are volitional, in that they may be altered by an individual's motivation, which may allow repeat test variation.

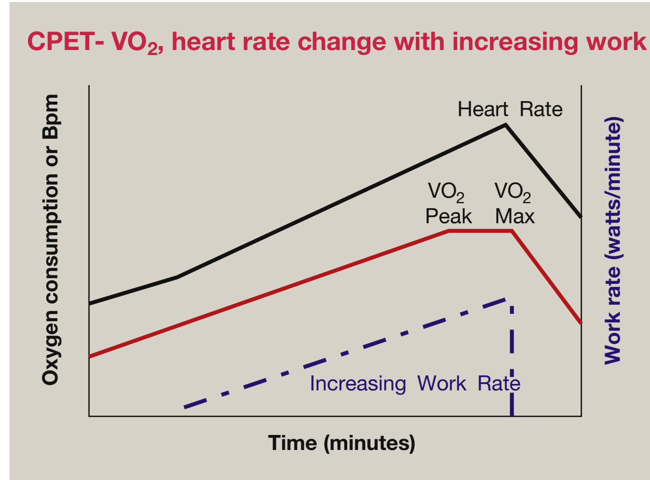

Figure 1

Anaerobic threshold: the ventilatory anaerobic threshold (VAT) represents a gaseous marker of the onset of systemic metabolic acidosis and the potential for cellular dysfunction. This is often reported as VO_2 in ml/kg/minute at the point at which anaerobic metabolism commences. While the cellular basis in aerobic and anaerobic metabolism is firmly established, there remains debate over the relationship of oxygen delivery versus utilization in causation of lactic acidosis and even in the sources of the total lactic acid load.[10] The VAT measured by gaseous exchange methodology represents the summary point of several potential processes centred around the change from aerobic to anaerobic metabolism.

VAT can be determined from various measured parameters but the most common initial methodology in the preoperative context is through the V-slope. When VO_2 is plotted against VCO_2 during ramped exercise, the VAT is reached as the gradient of the line VO_2/VCO_2 line moves away from unity. The initial point at which the gradient change occurs indicates the VAT. This is illustrated in Figure 2. Further simultaneous changes in ventilatory equivalents (VE/VCO_2 and VE/VO_2) and end-tidal PO_2 can assist in confirming the value of the AT (see below).

AT is an objective, non-volitional end-point and has been shown to be an independent predictor of postoperative complications[3] and indicative of increased risk of mortality in the elderly population.[2] VAT may vary depending on the modality and muscle groups used for exercise (e.g. AT is lower when performed on a cycle ergometer than on a treadmill).

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