Cardiopulmonary exercise testing: an overview

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Background

Historically, exercise tolerance testing (ETT) has provided clinicians with valuable diagnostic and prognostic information in the assessment of the patient with cardiac disease. More recently, with the emergence of advanced cardiac imaging modalities (i.e. nuclear imaging, stress echocardiography and MRI), the limitations of ETT in the detection of coronary ischemia have all but confirmed its inevitable demise. Clinical decision making from ETT relies predominantly on the interpretation of the ECG and patient reported symptoms in relation to an increasing exercise workload. Cardiopulmonary exercise testing (CPEX) offers a superior evaluation of a patient's integrated cardiovascular, respiratory and metabolic response to exercise by combining the standard measures of electrocardiography, blood pressure, O_2 saturation and exercise workload with ventilatory gas exchange data. Generally performed on a static bike, patients are required to wear a small facemask which enables the analysis of respired gases for the real-time, breath by breath determination of oxygen uptake (VO_2), carbon dioxide production (VCO_2) and minute ventilation (VE). Collective observation of the relationship between these variables, and their comparison to population norms, offers a unique insight into the cardiovascular, pulmonary and metabolic response to exercise. Conducted over a test duration of 9-12 minutes, CPEX utilises a ramp protocol which involves a gradual and continuous increase in workload at a rate of 5-15 watts/minute in clinical populations. The patient is required to exercise until either fatigue, or the development of clinical symptoms, prevents continuation.

Figure 1 – patient on bike

Clinical indications for CPEX

With vast improvements in technology, the utility of CPEX has evolved rapidly over the past decade from relative ambiguity as a research tool, to an ever more present and broadly applicable assessment in clinical practice. Currently its use extends to differential diagnosis in the exercise intolerant patient, assessment of perioperative risk prior to vascular and other surgeries, determination of prognosis and eligibility for cardiac transplant in CHF, and for effective prescription in exercise rehabilitation. Ultimately, in conjunction with other clinical assessments, it ably contributes to the holistic management of patients with complex disease. Within the field of cardiology in the UK, CPEX is under-utilised, most commonly conducted to establish clinical status in the CHF patient rather than to quantify the impact of coronary disease. In this regard, CPEX offers compelling diagnostic and prognostic information, and is equally effective in the assessment of the therapeutic benefit of pharmacological, electrophysiological or rehabilitative intervention. Recent data, also confirms increased sensitivity and specificity in the detection of coronary ischemia, over and above that of standard ETT. With the current trend in cardiac imaging it appears unlikely that CPEX will be widely adopted for the diagnosis of coronary ischemia in the near future but it should not be overlooked when considering that it is vastly cheaper, quicker and significantly less invasive than current tests. CPEX also has undoubted potential for the prescription of metabolic threshold based exercise in cardiac rehabilitation. There is considerable support for the notion that more accurate and effective exercise interventions may be delivered when prescription is determined by carefully measured metabolic gas exchange parameters as opposed to heart rate threshold altenatives.

Table1:

Clinical indications for CPEX
Differential diagnosis in patients with exercise limitation
Assessment of perioperative risk
Grading severity and establishing prognosis in heart failure
Assessing need for cardiac transplant
Assessing efficacy of therapeutic intervention
Exercise prescription for rehabilitation

The physiology of exercise

In order that the true value of CPEX may be appreciated, an understanding of the underlying physiological response to exercise is useful. The completion of sustained muscular work is reliant on the delivery of O_2 to the working muscle. The presence of O_2 at the muscle mitochondria, allows adenosine triphosphate (ATP) to be enzymatically split to release energy for exercise. Skeletal muscle stores of ATP are limited, and thus O_2 is further required during cellular respiration for the ongoing resynthesis of ATP from carbohydrates and fats. The CO_2 produced as a by-product of cellular respiration is comfortably ventilated during moderate intensity aerobic exercise. With increasing exercise intensity, however, energy production becomes more reliant on anaerobic pathways. A much increased ventilatory drive is required to expel additional CO_2 produced by bicarbonate buffering during lactic acidosis that results from the anaerobic resynthesis of ATP. The combined effects of lactic acidosis, in particular muscular fatigue, ensure that exercise becomes uncomfortable and ultimately unsustainable. Therefore, the transport and utilisation of O_2 is key to the successful completion of exercise. In order for this to be optimised, the integrity of the heart, lungs, blood vessels and the blood must be maintained. Inadequacy in any one or any combination of these factors will limit the efficiency with which exercise can be performed.

External respiration is tightly coupled to cellular respiration

Maximal oxygen consumption during exercise (VO_2 max) is an integrated measure of cardiorespiratory fitness and a powerful predictor of disease morbidity and mortality. Essential to the achievement of an appropriate VO_2 max, is a good cardiac output, a healthy blood oxygen concentration, an efficient distribution of blood to the working muscles and refined O_2 extraction at the muscle. External respiration, i.e. VO_2 and VCO_2 measured at the mouth by CPEX, is inextricably linked to cellular respiration (described above) thus providing a 'window' into O_2 delivery and utilisation by the muscle and CO_2 production and delivery to the lungs. When this data is combined with measurement of minute ventilation, heart rate and workload, the performance and competence of the organ systems coupling cellular and external respiration can be assessed. This allows CPEX to differentiate between exercise limitation caused by cardiovascular or respiratory disease and even to distinguish between different cardiovascular diseases. For example, chronic heart failure, coronary artery disease and peripheral vascular disease all have unique CPEX data profiles. It should be noted that skilled interpretation of CPEX results is required when considering differential diagnosis, and the addition of the more invasive measurement of arterial blood gases during CPEX significantly increases the accuracy of some diagnoses.

Figure 2 - wasserman diagram of the integrated physiological response to exercise

Summary: the role of CPEX in the NHS

Through the analysis of the relationship between external and cellular respiration, CPEX provides an integrated assessment of the multiple organ systems required for the completion of physical exercise. The evaluation of physiological function during exercise has the ability to unmask pathology which is otherwise occult when investigated at rest. In an increasingly comorbid population, the use of CPEX as a first line investigation offers a cheap, quick and comparatively less invasive modality for the simultaneous assessment of multiple organ systems. Completion of CPEX offers the physician the potential to assess multiple organ competence with a single test, isolating and/or excluding pathology, thus efficiently directing future investigations and avoiding needless additional tests. Not only does this reduce the impact on the patient, but it provides a cost effective solution for the NHS, reducing the financial burden of multiple investigations. In cardiology specifically, CPEX has an established place in the systematic assessment for cardiac transplant. Potential exists for a broader remit whereby CPEX could be used for the detection of coronary ischemia, which if confirmed as sufficiently accurate in future studies, would provide a compelling alternative to invasive and expensive nuclear imaging. Relatively speaking, the use of CPEX in clinical practice is still in its infancy, but it is highly likely that its application will become ever more frequent.