

# Cardiopulmonary Exercise Test (CPET): Background, Applicability and Interpretation

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**Background:** People are usually breathless when they are doing something, so it makes sense to assess their symptoms and **make physiological measurements during exercise** rather than rely on investigations performed at rest. Cardiopulmonary exercise testing is, therefore, an excellent way to work out why someone is breathless and to quantify their limitation.

A cardiopulmonary exercise test (CPET) involves measurements of cardiac and respiratory function whilst the subject exercises up to their maximum capacity.

A CPET can be a useful tool for diagnosing heart and lung disease, working out why someone is breathless, quantifying fitness, and predicting outcomes.

Preoperative CPET testing allows stratification of surgical risk and planning post-operative care.

## What is a CPET?

In a cardiac exercise test, a patient with known or suspected coronary artery disease exercises on a treadmill whilst their electrocardiogram (ECG) is primarily monitored for ST-segment changes. 'Cardiopulmonary' exercise tests go a step further by attaching a mask (or mouthpiece) to record breathing. This gives lots more information, not just about the lungs and heart, but also about the circulation and leg muscles. It also enables the estimation of work capacity and overall motivation to perform an exercise.

### Main components of CPET measurements

- The volume of air breathed in and out (minute ventilation, or VE)
- The volume of oxygen ( $O_2$ ) used up by the body (oxygen uptake, or  $VO_2$ )
- The volume of carbon dioxide ( $CO_2$ ) produced (carbon dioxide output, or  $VCO_2$ )
- Heart rate (HR)

**Three more parameters can be derived by combining two of these measurements:**

1. The respiratory exchange ratio (RER) i.e.,  $VCO_2/VO_2$ ,
2. Oxygen ( $O_2$ ) pulse i.e.  $VO_2/HR$  to some extent Stroke Volume (SV), and
3. Ventilatory equivalents (Ve<sub>q</sub>) i.e.,  $VE/VO_2$  and  $VE/VCO_2$ .

These parameters are also used to obtain a couple of useful thresholds: the anaerobic threshold (AT) and respiratory compensation point (RCP) i.e., the onset of hyperventilation ("respiratory compensation") when acidemia takes over from  $CO_2$  as the stimulus for

ventilation during incremental exercise. So, CPET interpretation, at an introductory level, only requires an understanding of fewer than ten parameters.

## Why do a CPET?

Most patients with cardiac or respiratory problems have symptoms that are worse on exertion, whereas many diagnostic tests are performed with a patient sitting in a chair or lying on a couch. It makes much more sense to undertake some physiological measurements when someone is doing an activity. A CPET puts the cardiac and respiratory systems under stress so that the capacity and reserve of the body can be assessed, particularly in terms of its ability to deliver O<sub>2</sub> to the exercising muscles.

## Things to do before you consider a CPET

Before a diagnostic CPET, a detailed history and clinical examination are mandatory. A few basic tests, such as a chest X-ray, ECG, hemoglobin (Hb) concentration, and renal function, should have been performed, and also arterial blood

### Indications for doing a CPET

CPET is a useful tool for:

- Finding out what is wrong with a patient who is short of breath on exertion
- Assessing the contribution of cardiac or respiratory pathologies to incapacity
- Quantifying the extent of any impairment and thus the prognosis
- Assessing the risk to the patient of any potential surgical procedure
- Measuring the response to any intervention

These preliminaries are important. Whilst it may be possible to assume from CPET results that the patient might be anemic or have renal failure, intermittent claudication, or muscle disease, there are other (better) ways of working this out. Overall, **a CPET rarely gives a definitive diagnosis and usually only helps direct clinicians towards a possible group of clinical conditions (e.g., conditions causing ventilatory limitation or cardiac impairment)**. Like any test, a CPET is probably best viewed i.e., if you suspect a problem, then a CPET can help to confirm or disprove your suspicions.

## Safety and the pre-test assessment

CPET is a safe test; in one series of 70,000 tests, no deaths occurred and only six major complications were encountered.

### Steps in the CPET process

- The clinical decision to undertake a CPET
- Pre-test assessment
- The CPET itself
- Interpretation of the results

### Risks that may develop during CPET test

- Myocardial infarction
- Arrhythmia
- Hemodynamic instability
- Bronchospasm
- Hypoglycemia
- Musculoskeletal injury
- Hyperventilation ± syncope

### Things to do before you consider a CPET

Prior to a diagnostic CPET, a detailed history and clinical examination are mandatory. A few basic tests, such as a chest X-ray, ECG, hemoglobin (Hb) concentration, and renal function, should have been performed, and also arterial blood gases if there is any clinical suspicion of respiratory failure or a low resting peripheral O<sub>2</sub> saturation (SpO<sub>2</sub>).

This is still vital that before any CPET, contraindications are checked and patient safety is prioritized. The decision to proceed with a test is at the carefulness and decision of the supervising/responsible clinician. We need to be aware of the risks involved and the side effects or problems that can occur. In our experience, the most common adverse events that occur are dizziness and collapse, arising from hyperventilation or vasovagal reactions if blood sampling is undertaken.

### The day of the test

Before starting the test, we must double-check the indication and check the risks. We will come back to the pre-test ECG shortly. If there is any possibility of exercise-induced asthma, check the forced expiratory volume in one second.

### Contraindications to CPET

- History of exercise syncope or pre-syncope
- Mental impairment, with an inability to co-operate with the test procedure
- Musculoskeletal problem limiting exercise capacity
- Acute coronary syndrome/myocardial infarction within last seven days
- Unstable angina
- Poorly controlled New York Heart Association (NYHA) class III or IV heart failure
- Symptomatic severe aortic stenosis
- Uncontrolled arrhythmia with hemodynamic compromise
- Aortic dissection
- Aortic aneurysm
- Acute asthma/exacerbation of COPD
- Pulmonary oedema
- Respiratory failure [arterial O<sub>2</sub> partial pressure (PaO<sub>2</sub>) <8 kPa]
- Severe pulmonary hypertension
- Acute pulmonary embolism

- Recent deep vein thrombosis
- Pulmonary arterial hypertension
- Frailty
- History of syncope/seizures

(FEV1) and make sure that a subject's asthma is no worse than when the test was requested; it would be inappropriate to proceed with the test during an exacerbation or acute illness; there is also a risk that strenuous exercise undertaken during a viral illness can lead to cardiac damage. Moreover, if the result shows an abnormal result, then it is actually very difficult to interpret the findings.

It is important that you re-schedule the test if the patient has got any risk factors at the present situation.

#### **Practical tip**

*If a patient is prescribed a regular medication, then there will often be a question as to whether this medication should be taken on the day of testing. Generally speaking, patients should be advised to take all of their usual medications—this is especially true if a patient is developing symptoms despite the use of medications (e.g., for asthma). Certain drugs will impact subsequent interpretation (e.g., beta-blockers), but providing they are listed and known, this is not a problem. Moreover, discontinuing cardiac medications suddenly can increase the risk of an adverse event during the test.*

#### **Technical point 1**

*Supervising a CPET yourself is much more informative than simply reviewing the printed results. Being present during the exercise provides a vast amount of insight as to the cause of an individual's exercise symptoms and any limitations.*

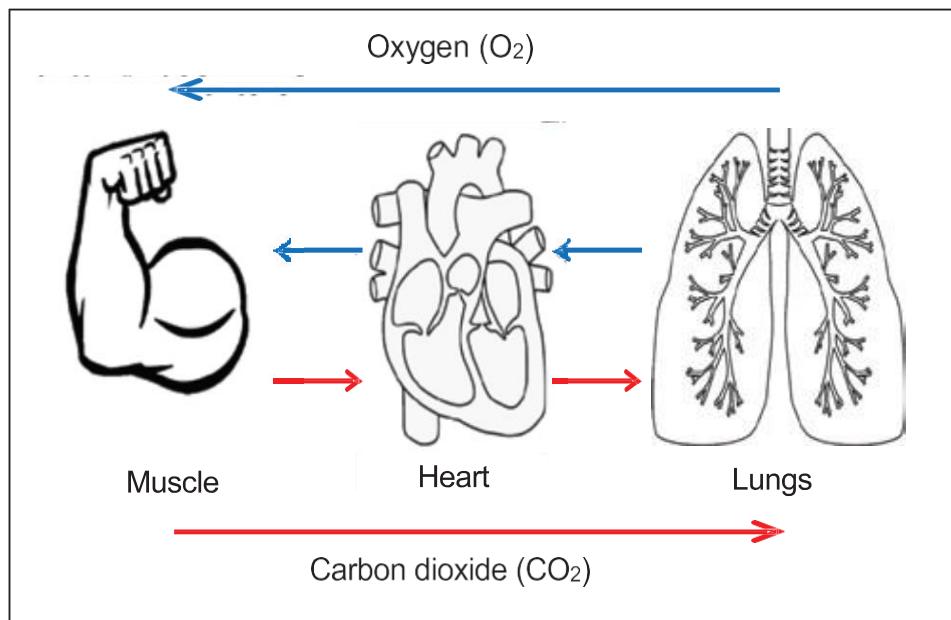
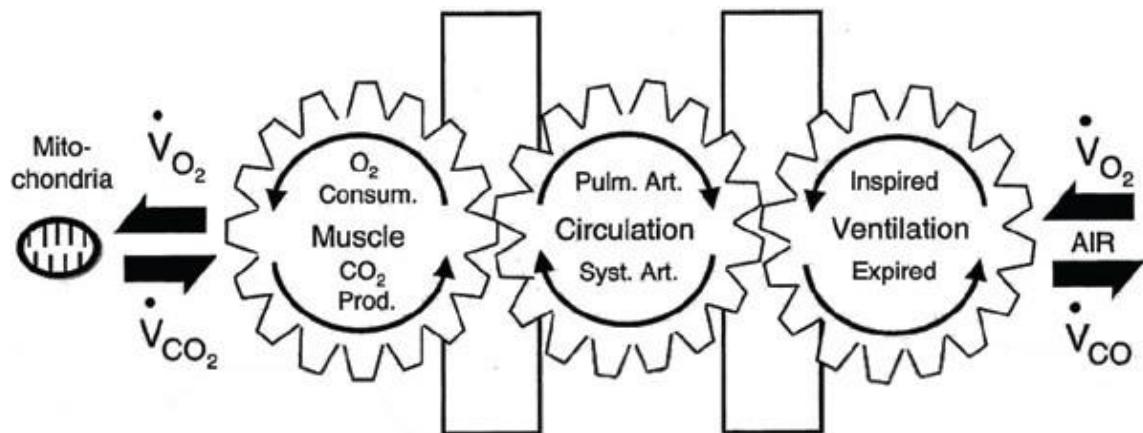
#### **NOTES:**

*Ventricular ectopics which are present on a resting ECG often disappear on exercise. If they start to occur in runs ± increase in frequency, then stop the test.*

**Applicability:** For utilization of O<sub>2</sub> and production of CO<sub>2</sub> the following 4 important machines are operating in our body, such as:

1. Lung for Ventilation and gases (O<sub>2</sub> and CO<sub>2</sub>) transfer,
2. Heart for pumping blood for carrying Oxygen and carbon-di-oxide,
3. Circulation and Hemoglobin for gases transport from Lung via the heart to Mitochondria, and
4. Muscle and Mitochondria for final oxygen utilization energy and CO<sub>2</sub> production.

We are doing CPET to measure the probable and specific site responsible for breathlessness, Preoperative assessment of operative risk after major surgery, for the purpose of assessment before and after Cardio-Pulmonary Rehabilitation program, and monitoring of Diseases during and after treatment.



**Interpretation:** Understanding and interpretation of 9 plots are very much important. It looks very clumsy, but after understanding, it looks very interesting. Start to see **panel 3** for  $\dot{V}O_2$ ,  $\dot{V}O_{2\text{ max}}$ ,  $\dot{V}CO_2$  and Load. If it is normal, then other plots would be normal. If  $\dot{V}O_{2\text{ max}}$  is less than 80% of predicted, then look at **panel 2** for heart rate and  $\dot{V}O_2/\text{HR}$  (Oxygen Pulse). Oxygen Pulse is the shadow of Stroke Volume. Horizontal or Linear Oxygen pulse and if it is less than 10ml/min and a vertical rise of HR indicating Cardiac origin shortness of breath. If VE is Vertical in **panels 1 and 4** and in **panel 7** VE touches 80% of MVV indicating Ventilation limitation is the cause of shortness of breath. **Panel 8** is for Respiratory Exchange Ratio (RER) i.e.  $\dot{V}CO_2/\dot{V}O_2$  is usually 0.8 at rest and it is reflecting whole-body metabolism. If it crosses 1.15 or more then it indicates Exercise is maximum and optimum. The early rise of RER

indicates Ventilation/Perfusion mismatch in heart or lung diseases. Heart rate (HR) is also more than 80% predicted in **panel 2** and workload up to threshold level in **panel 3** indicating exercise performance is maximum and optimum. **Panel 6** is an interesting Plot where we can measure Ventilatory Equivalent  $\text{VO}_2$  and Ventilatory Equivalent  $\text{VCO}_2$  by simply measuring  $\text{VE}/\text{VO}_2$  and  $\text{VE}/\text{VCO}_2$ .  $\text{VeQO}_2$  falls during the early phase of a CPET as cardiac output increases, so that perfusion (Q) and ventilation (V) matching become more even.  $\text{VeQC}O_2$  values as an index of severity of the disease. *If the  $\text{VeQC}O_2$  does not fall below 30 (or lower in young individuals), this implies that there is something wrong with gas exchange in the lungs (with a high  $Vd/Vt$  ratio). The best example of this is seen in pulmonary vascular disease.*

$\text{VeQO}_2$  rises beyond the AT, when increased production of  $\text{CO}_2$  (from buffering of lactic acid) leads to an increase in ventilation out of proportion to the increase in  $\text{VO}_2$ . **Panel 9** is an indirect measurement of Blood gases by measuring  $\text{SpO}_2$ , End Tidal  $\text{PO}_2$  ( $\text{etPO}_2$ ) and End Tidal  $\text{PCO}_2$  ( $\text{etPCO}_2$ ) levels.

The following step is the analysis of  $\text{O}_2$  saturation. A drop of  $\text{SpO}_2$  greater than 4% on peak exertion as compared to resting is characteristic of pulmonary limitation. High  $\text{VE}/\text{VCO}_2$  slope and  $\text{PETCO}_2 < 33 \text{ mmHg}$  at rest and/or elevation greater than 8 mmHg during exertion suggest respiratory mechanisms as the cause of dyspnea.<sup>3,63</sup> Observation of  $\text{O}_2$  pulse and  $\Delta\text{VO}_2/\Delta\text{HR}$  ratio can identify heart disease, if the curves show plateau or decline, reflecting an inadequate SV to the load imposed.<sup>64</sup> However, individuals with lung disease and some degree of pulmonary hypertension can also develop a plateau of  $\text{O}_2$  pulse. The combination of the plateau of  $\text{O}_2$  pulse with a decrease in  $\text{O}_2$  saturation,  $\text{VE}/\text{VCO}_2$  slope  $> 40$  and reduced  $\text{PETCO}_2$  ( $< 33 \text{ mmHg}$  at rest or  $< 36 \text{ mmHg}$  at AT) strongly suggests pulmonary hypertension or pathology with pulmonary vascular impermeant. *The  $\text{HR}/\text{VO}_2$  plot is probably one of the most important plots in the interpretation of CPET. Look at it early in any interpretative strategy, and plot out and compare the expected trajectory with your patient's result in panel 5.* This then allows you to evaluate if the HR: (i) is high at rest; (ii) follows a normal profile but stops early (e.g. in lack of effort); (iii) has a sudden kick-up (e.g. in the onset of cardiac ischaemia); (iv) is depressed (Fig. 6.7); or (v) is steep and stops because of left ventricular dysfunction.

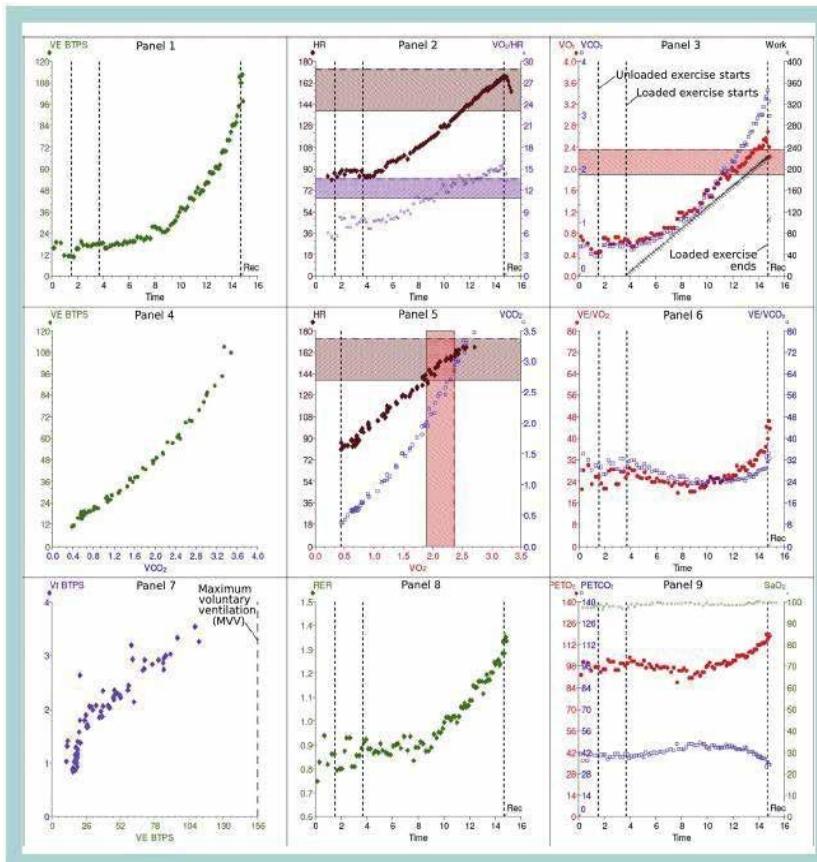
## End-tidal $\text{O}_2$ and $\text{CO}_2$ values

The majority of CPET equipment will display live data for end-tidal  $\text{O}_2$  ( $\text{etO}_2$ ) and  $\text{etCO}_2$ . The idea is that the gas exhaled right at the end of expiration has come from deep within the lungs, i.e. from the alveoli (Fig. 11.6). This will be a mixture of gas from all alveoli, some of them well perfused and some under-perfused. In healthy individuals,  $\text{etO}_2$  and  $\text{etCO}_2$  change very little during a CPET.

During the early part of a CPET, more and more  $\text{O}_2$  is taken up from the alveoli into the blood, as V–Q matching improves. As a result, there is less  $\text{O}_2$  in the expired gas. In other words, the  $\text{etO}_2$  falls slightly (Fig. 11.7).

Past the AT, however, ventilation increases without any more  $\text{O}_2$  being taken up by the blood. As a result, the expired gas starts to look more like inspired air, so the end-tidal level rises again, back towards that of inspired air.

In healthy individuals (i.e. with normal dead space matching), the etCO<sub>2</sub> can be used to estimate the PaCO<sub>2</sub>, and this assumption is used by many CPET software systems to provide a Vd/Vt value. In the presence of any lung disease (i.e. the exact time when you may wish to detect a problem with Vd/Vt), this relationship is far less reliable and thus arterial blood gas measurement is recommended. In fact, measuring the difference between PaCO<sub>2</sub> and etCO<sub>2</sub> at peak exercise can provide valuable insight into the integrity of the pulmonary vascular interface; the PaCO<sub>2</sub>-etCO<sub>2</sub> difference should be negative in normal individuals at peak exercise and this is a useful way of checking there is no problem with lung 'efficiency' or a high dead space.



### A stepwise approach to interpreting CPET data

Step	Graph
A: Accuracy—is the test valid?	Review all graphs
B: Best effort—did they push themselves?	VO <sub>2</sub> vs time or HR (for VO <sub>2</sub> max, and occasionally VO <sub>2</sub> plateau)

	HR vs time (for reserve)
	VE vs time (for reserve)
	VCO <sub>2</sub> vs VO <sub>2</sub> (for AT)
	RER vs time (for peak value)
	VE vs VCO <sub>2</sub> (for RCP)
C: Capacity—is it impaired?	VO <sub>2</sub> vs time or HR (for VO <sub>2max</sub> )
D: Determine what limited exercise	VE vs time (for reserve)
	HR vs time (for reserve)
	HR vs VO <sub>2</sub> (for HR rise)
	O <sub>2</sub> pulse vs time (for heart disease)
	SpO <sub>2</sub> vs time (for lung disease)
E: Extra value	AT, Veq, RER, VE/Vt, airflow limitation, IC
F: Finish	Review all graphs

## Anaerobic Threshold

### Key points

- A long-standing concept in CPET is the presence of a 'threshold' during progressive incremental exercise, termed the anaerobic threshold (AT).
- Although controversial, the AT is thought to represent a point during CPET where anaerobic processes increasingly supplement aerobic metabolism, with increasing production of lactic acid.
- Lactic acid is buffered by HCO to produce more CO<sub>2</sub>.
- The AT should occur when the VO<sub>2</sub> is >40% of an individual's predicted VO<sub>2max</sub>.
- A low AT is primarily caused by impaired O<sub>2</sub> delivery to muscles, usually because of heart disease or peripheral vascular disease.

## Oxygen Saturation:

A fall in O<sub>2</sub> saturation >4% occurs in some patients with severe lung ± pulmonary vascular disease when they start to do even minimal exercise. Clearly, this will be immediately evident if they are assessed during a progressive CPET. A significant fall in SpO<sub>2</sub> during the test is, however, generally pretty unusual and should be taken seriously; potentially it indicates a worrying problem with gas exchange.

### The four main causes of genuine O<sub>2</sub> desaturation during a CPET

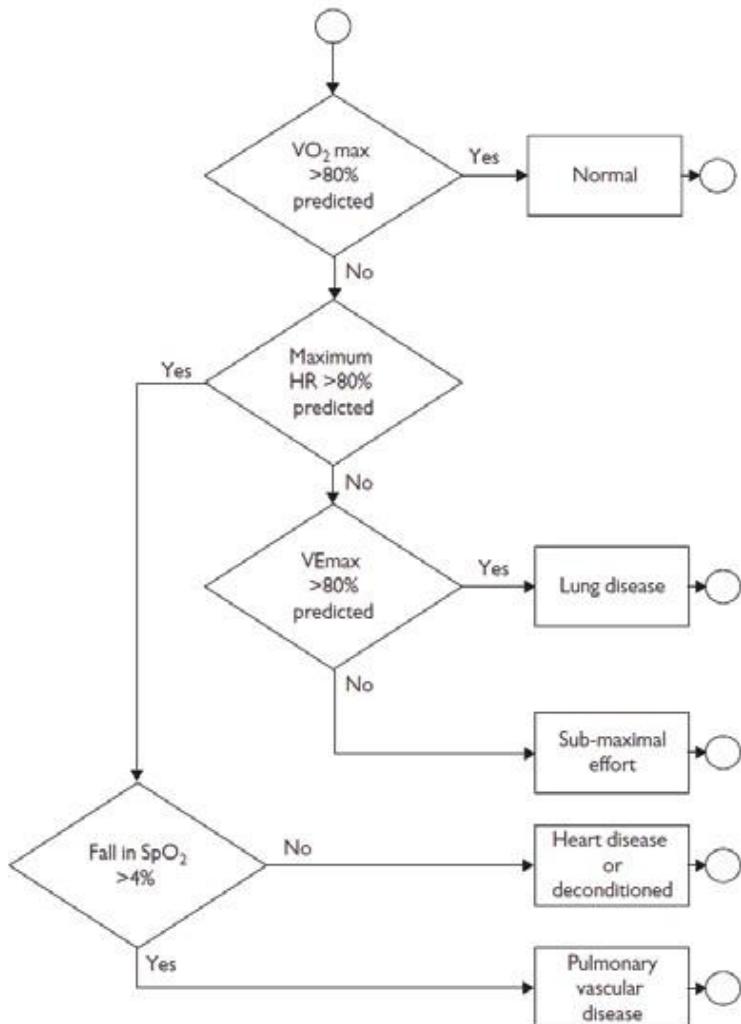
1. Ventilation-perfusion (V/Q) mismatch/inequality
2. Impaired diffusion
3. Right-to-left cardiac shunt
4. Alveolar hypoventilation, i.e. hypercapnia

A simple, yet systematic, and logical approach is needed for CPET reporting. If applied consistently, this should allow all but the most complex of problems to be detected reliably. It is rare, however, that CPET will give a definitive diagnosis. It usually provides general information on the problem area, e.g. there is a limitation with

ventilation ± gas exchange or delivery of O<sub>2</sub>/circulation.

Algorithms showing here can help guide you through the results and a systematic approach to interpretation is vital to ensure nothing is missed.

#### INTERPRETATION OF CARDIOPULMONARY EXERCISE TESTS



Example of an algorithm for CPET interpretation.

## 38 Learning Points from CPET

1. Most of the information we gain from a CPET is derived from just four key measurements and their relationship during incremental exercise.
2. Supervising a CPET yourself is much more informative than simply reviewing the printed results. Being present during exercise provides a vast amount of insight as to the cause of an individual's exercise symptoms and any limitations.
3. Adverse events during a CPET are very rare—all the more reason to prepare for them meticulously. 'Fail to prepare, then prepare to fail', as the old adage goes.
4. Ventricular ectopics which are present on the resting ECG often disappear on exercise. If they start to occur in runs ± with increasing frequency, then stop the test.
5. Slow recovery of the heart back to a normal rate once exercise ceases is an indicator of significant cardiac impairment.
6. Most CPET results will be breath-by-breath plots of a symptom-limited maximum test, during which the workload is steadily increased until the subject can no longer keep turning the cycle ergometer.
7. A  $\text{VO}_2\text{max}$  of  $<20 \text{ ml/kg/min}$  is low;  $<15 \text{ ml/kg/min}$  is moderate impairment of cardiorespiratory function; and  $<10 \text{ ml/kg/min}$  is severe impairment.
8. The expected normal value for  $\text{VO}_2\text{max}$  is 10–20% lower in females than in males and declines with age by around 10% per decade beyond the age of 30 years.  $\text{VO}_2\text{max}$  is dependent on the total muscle mass being used and thus it is greater in treadmill exercise when compared with bike exercise.
9. Generally speaking, a  $\text{VO}_2\text{max} >80\%$  predicted means that it is very unlikely that the subject has clinically significant pathology affecting their heart or lungs.
10. At peak exercise, a normal subject should reach 80% or more of their predicted maximum HR.
11. The HR/ $\text{VO}_2$  plot is probably one of the most important plots in the interpretation of a CPET. Look at it early in any interpretive strategy; plot out and compare the expected trajectory with your patient's result.
12. The  $\text{O}_2$  pulse can be used as an indirect indicator or a 'surrogate' of the cardiac SV.

13. A normal subject should achieve an  $\text{O}_2$  pulse of at least 10 ml/beat during a CPET.
14. If the  $\text{O}_2$  pulse reaches a plateau, suspect impairment of CO (due to heart disease or pulmonary vascular disease), particularly if the peak value is <10 ml/beat.
15. Predicted VEmax is measured for each subject individually, from the FEV1 or MVV, rather than taken from published normative tables.
16. Ventilation should not reach 80% of predicted during a CPET in a normal subject.
17. If  $\text{VO}_{2\text{max}}$  is low and ventilation exceeds 80% of predicted (i.e. there is a low ventilatory reserve), then there is probably something wrong with the pulmonary system.
18. During a CPET,  $\text{CO}_2$  comes from the oxidative metabolism of carbohydrates (aerobic metabolism) and from buffering the  $\text{H}^+$  of lactic acidosis (generated by anaerobic glycolysis).
19. Quick breathing is often described as 'hyperventilation'. Strictly speaking, physiologically, this term should only be used when ventilation is occurring in excess of metabolic demand and is associated with a reduction in  $\text{PaCO}_2$ . A general increase in ventilation is termed hyperpnea.
20. The RER ( $\text{VCO}_2/\text{VO}_2$ ) should be <1.0 in the early part of a CPET and rises above 1.0 as exercise progresses past the AT (and will continue to rise after exercise stops).
21. If the  $\text{VeCO}_2$  do not fall below 30 (or lower in young individuals), this implies that there is something wrong with gas exchange in the lungs (with a high  $\text{Vd}/\text{Vt}$  ratio). The best example of this is seen in pulmonary vascular disease.
22. A key reason the equivalents fall is because the equivalents actually represent the 'moment-by-moment' change in the gradient of the  $\text{VE}/\text{VCO}_2$  or  $\text{VE}/\text{VO}_2$  slope. So, if there is a positive intercept on these graphs (Fig. 9.2), i.e. the values do not go directly through the intercept, then as you plot the change in that gradient over time, the gradient of more distant points will be lower and when plotted against time will appear to be falling, irrespective of 'efficiency'. This is difficult to understand initially, but many of the derived or composite plots used in CPET panels need to be viewed in the context of mathematical plotting and the way graphs are created.
23. Aerobic metabolism continues beyond the AT but is supplemented by anaerobic processes.
24. Beyond the AT,  $\text{VCO}_2$  increases more steeply than  $\text{VO}_2$  and an inflection point is seen in the 'V-slope' when  $\text{VCO}_2$  is plotted against  $\text{VO}_2$ .
25. The AT should be 40% or more of the predicted  $\text{VO}_{2\text{max}}$ , not the actual  $\text{VO}_{2\text{max}}$ . If it is lower, then there is likely to be a problem.
26. The presence of a clear RCP implies the development of an additional drive to breathing caused by acidemia and the body's attempt to maintain pH.
27. In the presence of significant lung disease, a clear RCP may not be apparent.
28. A fall in  $\text{SpO}_2$  of >4% during a CPET is abnormal and implies the presence of lung disease, pulmonary vascular disease, or the opening of a right-to-left shunt.
29. A CPET is an excellent way of stressing the gas exchange capabilities of the lungs and unmasking diffusion limitation which may not have been apparent on tests done with the patient at rest. (It is also worth remembering that the corridor walking test may miss significant desaturation that is then subsequently revealed on a CPET.)

30. A PFO is present in up to one in four of the population and may only open up on exercise.
31. EIB is usually diagnosed when there is a  $\geq 10\%$  fall in FEV1 from the pre-test or baseline value in the 20 minutes' post-exercise. The PEFR is not a reliable marker of EIB as it is more effort-dependent and thus if the subject is tired following an exercise test, the PEFR will fall.
32. To interpret a CPET, you need summary data about exercise capacity in both tabular form and graphs to show you what happened on the way.
33. The nine-panel plot is the most frequently used way of displaying CPET results and many physiologists talk about, or ask for, the 'nine-panel'. This is simply a reference to obtaining a graphical review of the whole CPET.
34. In any erudite conversation regarding CPET, specialists will soon start to mention McArdle's syndrome, a rare inherited myopathy characterized by a lack of myophosphorylase. The condition is of particular interest because there is impaired glycolysis and thus a failure of lactate production. This results in early exercise cessation with a low VO<sub>2</sub>, a steep chronotropic response, a low RER, and no significant rise in lactate.
35. Hb is the key component in O<sub>2</sub> carriage, so anemia is associated with reduced O<sub>2</sub> content.
36. A low preoperative VO<sub>2max</sub> is associated with an increased risk of non-cardiac post-operative complications and death. The lower the VO<sub>2max</sub> (as % predicted), the higher the risk.
37. From a physiological viewpoint, a subject with a VO<sub>2max</sub> >80% predicted or >20 ml/kg/min can probably be considered as low risk for surgery. A VO<sub>2max</sub> <15 ml/kg/min is often cited as a threshold for increased risk.
38. If an exercise prescription is going to be successful, then the first important step is to discuss what an individual wants to achieve, i.e. establishing the patient-selected goals.

#### **Reference:**

A Practical Guide to the Interpretation of Cardiopulmonary Exercise Tests, SECOND EDITION Kinnear W.J.M. Senior, Nottingham Trent University, UK, Hull J H., University College London, UK, Oxford University Press 2021 Library of Congress Control Number: 2020952574 ISBN 978-0-19-883439-7. DOI: 10.1093/med/9780198834397.001.0001