Cardiopulmonary Exercise Test: Interpretation and Application in Perioperative Medicine

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KEY POINTS

- Cardiopulmonary exercise tolerance testing (CPET) is useful in predicting perioperative risk.
- It aids multidisciplinary team (MDT) decision making and facilitates informed consent.
- During CPET, measurements of oxygen (O_2) consumption, carbon dioxide (CO_2) production and ventilatory changes during a ramped increase in exercise are made, whilst noninvasive O_2 saturations (SpO_2), blood pressure (BP) and an electrocardiogram (ECG) are continuously recorded.
- The peak O_2 consumption, anaerobic threshold and ventilatory equivalents for CO_2 are suggested predictors of postoperative mortality in a variety of surgical procedures.
- A patient's CPET performance provides a prehabilitation baseline, which guides preoptimisation strategies.
- Under the governance of the Perioperative Exercise Testing and Training Society (POETTS), CPET provision has been standardised to achieve high-quality, reliable and comparable data.

INTRODUCTION

Cardiopulmonary exercise tolerance testing (CPET) is a dynamic, noninvasive assessment of the cardiopulmonary system at rest and during exercise, performed preoperatively to determine functional capacity. Questioning a patient regarding their exercise tolerance is part of a routine preoperative assessment and provides an indication of a patient's comorbidity and frailty. CPET goes further to quantify the degree and nature of physiological deficit based on the pattern of deviation from the norm within CPET data.

We will examine key CPET variables, explore common patterns of physiological deviation by exercise-limiting pathology and then explain how to use these results to plan the perioperative journey. An in-depth review of physiological response to exercise is not provided in this tutorial. It is, however, useful to revise the Fick equation to understand how O_2 consumption ($\dot{V}O_2$) can be calculated from CPET measurements. A widely accepted definition of the Fick principle states, 'The total uptake or release of a substance by peripheral tissues is equal to the product of the blood flow to the peripheral tissues and the arterio-venous concentration difference of the substance'[1].

$$\dot{V}O_{2\,max} = HR_{max} \times SV_{max} \times a\text{-}vO_2 difference_{max},$$

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TAKE ONLINE TEST

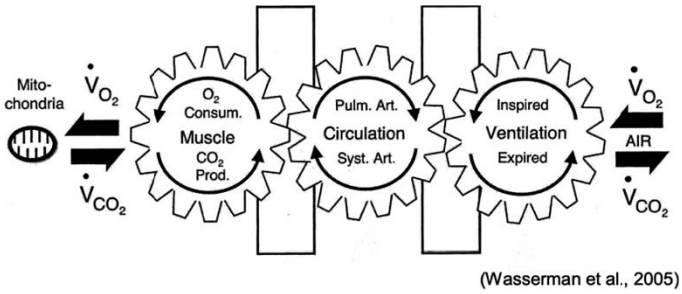

Figure 1. This well-known diagram by Wasserman illustrates these 5 stages. $\dot{V}O_2$ = rate of O_2 uptake, $\dot{V}CO_2$ = rate of CO_2 production. In reality, the body is not in a steady state. Permission to use image granted by the publisher for Wasserman et al.[2]

where $\dot{V}O_2$ is the total O_2 consumption per unit time, HR is heart rate, SV is the volume of blood ejected from the left ventricle during each systolic contraction and a-vO_2 is difference in the arterial and venous O_2 content. During CPET, an indirect Fick method is used that includes estimations of SV based on the patient's demographics and measurements of inspiratory and expiratory O_2 concentrations.

EXERCISE TOLERANCE

To achieve a normal exercise tolerance, the body needs to adequately achieve the following:

- Ventilation
- Gas exchange
- Delivery of oxygenated blood to exercising tissues and return of CO_2 to the lungs
- Extraction of O_2 by the muscle and transfer of CO_2 to the blood
- Appropriate use of O_2 within mitochondria to generate energy as adenosine triphosphate (ATP)

O_2 consumption ($\dot{V}O_2$) is the amount of O_2 taken in and used by the body per unit time and is thus the rate of O_2 use. CO_2 production ($\dot{V}CO_2$) is the amount of CO_2 exhaled from the body per unit time (see Figure 1).[2]

Increased $\dot{V}O_2$ by the muscles results from increases in the following:

- O_2 extraction from the blood at the exercising muscles
- O_2 delivery, by a decrease in local vascular resistance
- Cardiac output, through increased heart rate and stroke volume
- Pulmonary blood flow
- Linear increase in minute ventilation through increased tidal volume and ventilatory frequency

At rest, $\dot{V}O_2$ is approximately 3.5 mL·kg^{-1}min^{-1}. During strenuous exercise, this can increase by more than 10 to 20 times, requiring a large cardiopulmonary response to deliver the required O_2 to the muscles (see Figure 2). Measuring $\dot{V}O_2$ is of particular interest during exercise because it reflects the needs of the body in a stressed, perioperative state. It is recognised that patients who are less physically fit are more likely to experience adverse perioperative outcomes.

CPET VARIABLES

A magnetically braked (or similar) cycle ergometer with a predetermined ramp of pedalling resistance provides a reliable, gradual increase in work rate (in Watts). A treadmill or hand ergometer is an alternative. The breath-by-breath expired gas concentrations are commonly measured using rapid infrared gas analysers, while flow is measured by pressure differential pneumotachographs. This enables calculation of $\dot{V}O_2$ and $\dot{V}CO_2$, together with spirometry and respiratory rate. Serial measurements of electrocardiogram (ECG), O_2 saturation (SpO_2) and blood pressure (BP) are also recorded. From the primary values of $\dot{V}O_2$, $\dot{V}CO_2$, minute ventilation ($\dot{V}_E$) and HR, secondary values can be calculated, such as ventilatory equivalents for CO_2 ($\dot{V}_E/\dot{V}CO_2$). These terms are explained below. Trends are represented graphically by computer software and displayed in a '9-panel plot', where the cardiovascular system is represented by panels 2, 3 and 5; ventilation is represented by panels 1, 4 and 7; and panels 6, 8 and 9 show ventilation-perfusion (VQ) relationships.

$\dot{V}O_2$ Peak

The $\dot{V}O_2$ increases linearly at a rate of 10 mL of O_2·min^{-1} for every 1-W increase in power.[3] Any level significantly lower than this could imply a limitation in the patient's physiological reserve. The limit of tolerated exercise is reached at a plateau threshold known as the maximum O_2 consumption ($\dot{V}O_{2max}$). In the case of an increasing ramp CPET, where a shorter duration

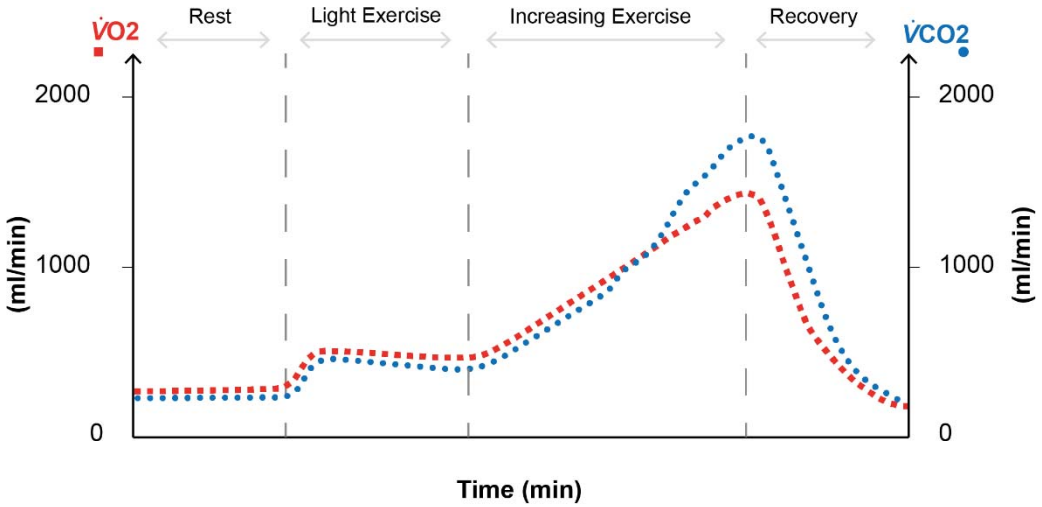

Figure 2. Normal response to exercise: at rest, our oxygen consumption ($\dot{V}O_2$) is approximately 250 mL·min^{-1} with a lower CO_2 production ($\dot{V}CO_2$) of varying fraction depending on diet. $\dot{V}O_2$ increases on light exercise such as slow walking, as does $\dot{V}CO_2$, proportionally. $\dot{V}O_2$ and $\dot{V}CO_2$ increase linearly with increasing work rate. Anaerobic metabolism then further increases CO_2 production without any further utilisation of O_2, illustrated here where trendlines cross.

of increasing work rate is used and where we would not be certain of a plateau threshold, we use the peak O_2 consumption ($\dot{V}O_{2peak}$). The $\dot{V}O_{2peak}$ is usually measured over a 20-second average of peak O_2 consumption (see Figure 3).

Research has elicited different $\dot{V}O_{2peak}$ thresholds of increased risk for different surgery types. In general, a $\dot{V}O_{2peak}$ of $<$15 mL O_2 kg^{-1}·min^{-1} is considered to represent an increased risk of perioperative complications.

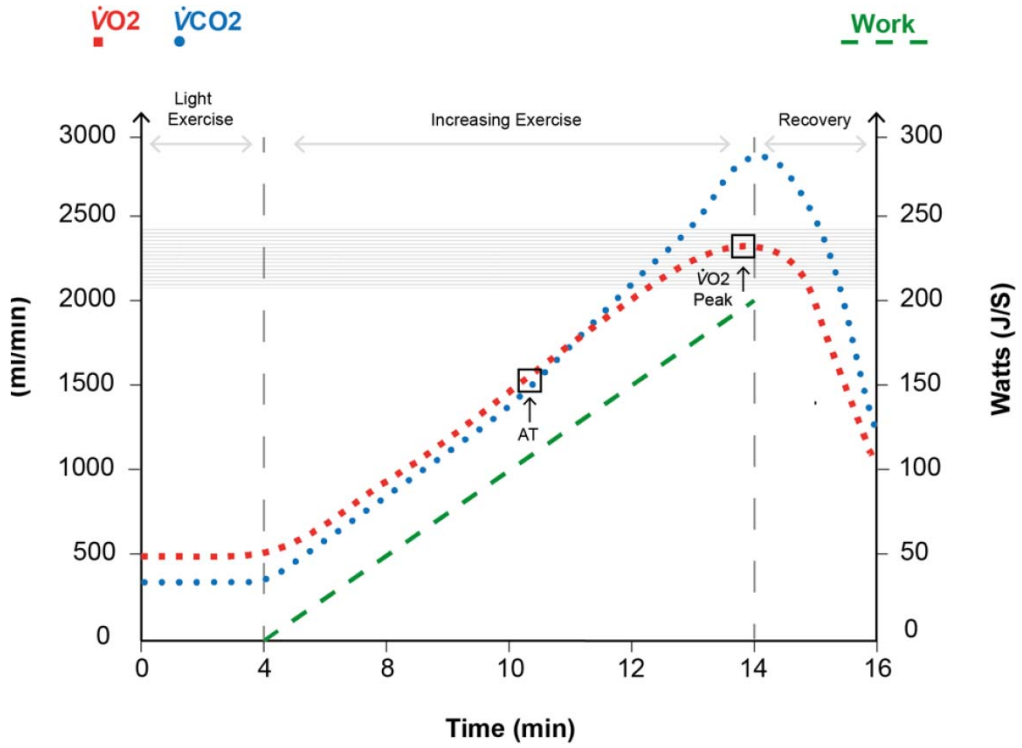

Figure 3. $\dot{V}O_2$peak: a 20-second-averaged maximum oxygen consumption is recorded during the peak of the subject's work rate. Typically, this will be the time preceding the transition to recovery or prior to stopping the test prematurely due to patient exhaustion. The $\dot{V}O_2$ peak recorded may be the patient's 'best effort'; however, it is not a physiological limit and is therefore not their highest attainable $\dot{V}O_2$. As work increases, if $\dot{V}O_2$ begins to plateau, this represents the highest attainable $\dot{V}O_2$ for a subject and is known as maximal $\dot{V}O_2$ or $\dot{V}O_2$ max. Noting the linear relationship between work rate and $\dot{V}O_2$, the increase in the $\dot{V}O_2$ (red squares) should parallel the increase in work (green dash). The horizontal shading indicates the patient's 80-100% predicted VO_2 peak given their demographics.

Anaerobic Threshold

The anaerobic threshold (AT) is the point at which the cardiopulmonary system is unable to meet the O_2 demand of the muscles. Muscle cells generate ATP by switching to anaerobic metabolism, a process that produces lactic acid. Lactic acid is buffered by our bicarbonate buffer system, and further CO_2 is generated.

CO_2 output will climb in proportion to O_2 consumption until the AT, at which point the change in $\dot{V}CO_2$ ($\Delta\dot{V}CO_2$) exceeds the change in $\dot{V}O_2$ ($\Delta\ \dot{V}\ O_2$). This can be seen on a 'V-slope' plot of $\dot{V}CO_2$ against $\dot{V}O_2$ (see Figure 4).

Values of AT indicating increased risk vary depending on the type of surgery. That said, an AT of $<$11 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$ would put the patient into a higher-risk group.[4]

Ventilatory Equivalents

These are indicators of ventilatory efficiency, representing the ratio of minute ventilation ($\dot{V}_E$) to CO_2 output or O_2 uptake. They provide us insight into the efficiency of VQ matching in the lung and that of gas exchange. If we consider the $\dot{V}_E$ required to support an increase in $\dot{V}O_2$ and $\dot{V}CO_2$, a lower $\dot{V}_E$ (and therefore a lower ratio) would represent greater efficiency.

Plotting the ventilatory equivalents for $\dot{V}O_2$ and $\dot{V}CO_2$ against time with increasing exercise intensity, we see a small initial improvement in the ventilatory efficiency. This is due to decreased dead space ventilation as the tidal volumes increase at the start of exercise (see Figure 5).

Beyond the AT, lactate produced is buffered by the bicarbonate system generating more CO_2, which acts on chemoreceptors and subsequently the respiratory center, increasing $\dot{V}_E$. Initially, there is an isocapnic buffering phase in which $\dot{V}_E/\ \dot{V}CO_2$ remains the same, but the $\dot{V}_E/\ \dot{V}O_2$ rises, as relatively no more O_2 is being consumed. The divergence of the $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\ \dot{V}CO_2$ lines at this point is another way of marking the AT. The $\dot{V}_E/\dot{V}CO_2$ at the AT is the value that is reported and is usually less than 34. The higher the level, the higher the perioperative risk.

INTERPRETATION OF CPET DATA

The test may be too physically demanding for the patient to generate adequate data for interpretation; however, the inability to complete a test is a useful measure in predicting poor surgical outcome.

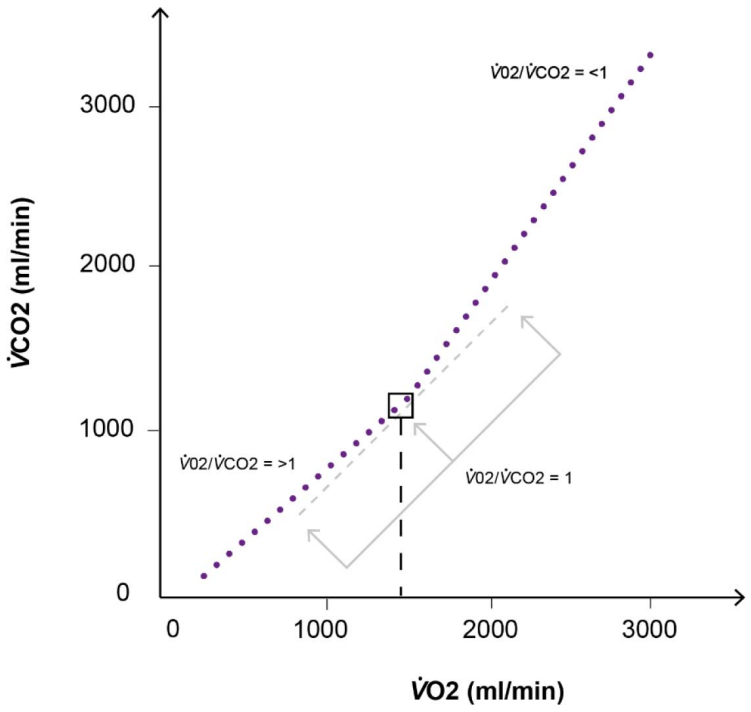

Figure 4. The 'V-slope' method plotting $\dot{V}O_2$ against $\dot{V}CO_2$. Initially, there is a steady rise in both parameters. At the anaerobic threshold, the $\dot{V}CO_2$ will increase in relation to the $\dot{V}O_2$, increasing the gradient of the curve. Wasserman's method was to plot a straight line of best fit through the initial and final parts of the curve. The intersection of these 2 lines would be the AT. The 'modified V-slope' method may also be used (shown). Here, a $\dot{V}O_2/\ \dot{V}CO_2 = 1$ gradient line is brought in from the right, and the point at which it touches the curve and the dots pull away from it with increasing gradient is the AT.

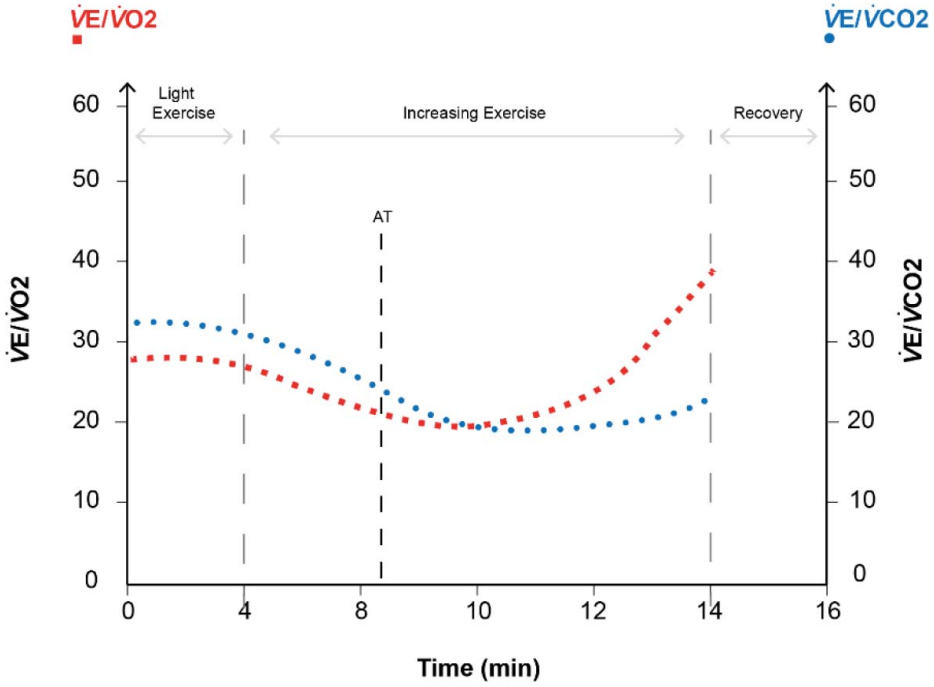

Figure 5. Ventilatory equivalents. AT is at the point at which divergence begins. Increased CO_2 production drives minute ventilation up, and therefore, while oxygen consumption remains constant, the $V_E/\dot{V}O_2$ ratio increases with respect to $V_E/\dot{V}CO_2$.

1. Was the test terminated prematurely?

Adapted from the American Thoracic Society, POETTS have consensus guidelines on the reasons for premature termination of the CPET.[5] These include the following:

- Angina: >2 mm ST depression if symptomatic or 4 mm if asymptomatic or >1 mm ST elevation
- Arrythmia causing symptoms or haemodynamic compromise
- Hypotension: systolic BP drop of >20 mm Hg from the highest value during the test
- Hypertension
  - Systolic BP >250 mm Hg
  - Diastolic BP >120 mm Hg
- Desaturation: SpO2 <80%
- Loss of coordination or mental confusion
- Dizziness or faintness

2. Is the test maximal?

The patient will usually stop when they are symptom limited and cannot exercise any longer. It is possible to grade their symptoms with a suitable scale, such as the Borg scale, at this point (see Figure 6) [6]. The reason for stopping must be ascertained, such as tired legs, dyspnoea, or pain. See Figure 7a,b for markers of a maximal test.

The respiratory exchange ratio (RER) is the ratio of $\dot{V}CO_2/\dot{V}O_2$ and corresponds to gas exchange. At a basal metabolic rate, it represents tissue metabolism and equates to the respiratory quotient (RQ). Metabolism of carbohydrate, protein and fat result in RQs of 1, 0.8 and 0.7, respectively. Because extra CO_2 is introduced into the system during anaerobic exercise from bicarbonate buffering of lactic acid, an RER substantially greater than 1 at peak exercise is one marker of maximal effort.

Physiological markers of a maximal test include the following:

- >80% predicted work rate (as per demographics)
- >80% maximal HR (predicted maximum = 220 beats·min^{-1} − age)
- Heart rate reserve (HRR) of <15% would indicate a maximal test, where HRR = predicted maximum HR − maximum HR achieved during the test; a raised HRR could represent a submaximal test or chronotropic insufficiency
- Achieving an RER >1.15
- Achieving maximal predicted $\dot{V}_E$.

Borg RPE	
Score	**Level of exertion**
6	No exertion at all
7	
7.5	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

Figure 6. Where RPE = rating of perceived exertion, the original scale was developed in healthy individuals to correlate with exercise heart rates (eg, RPE 15 would approximate a HR of 150 bpm).[7]

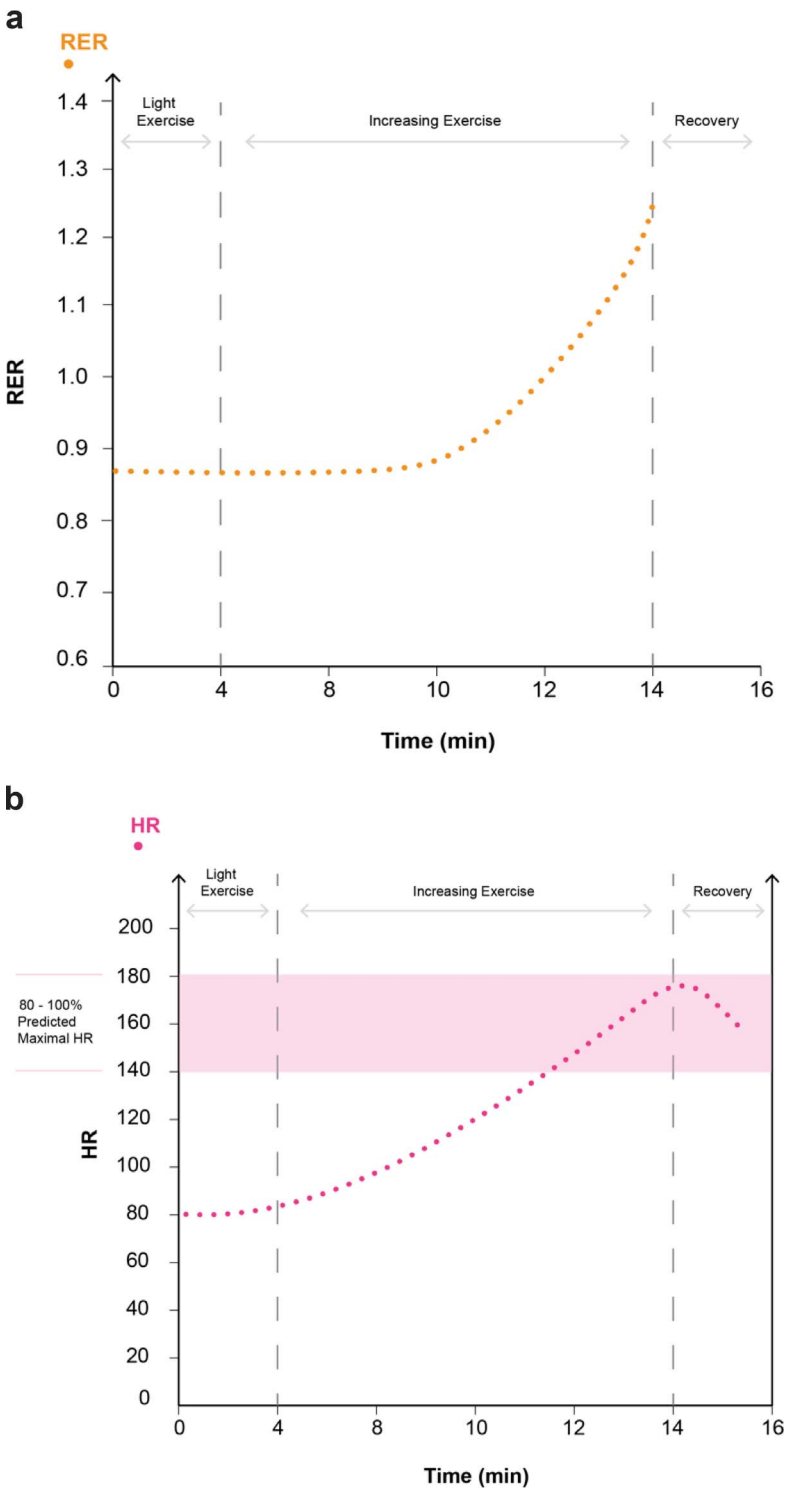

Figure 7. Markers of a maximal test. Increasing RER to >1.15 within the exercising period is indicative of a maximal test. Achieving >80% maximal HR as indicated by HR within the 80-100% predicted maximal HR reference zone is also indicative of a maximal test.

COMMON PATTERNS OF PHYSIOLOGIAL LIMITATION

We will now examine 3 common patterns of physiological limitation by exercise-limiting pathology (see Table) [7].

Cardiovascular Limitation

In individuals with valvular or ischaemic cardiac pathology, there is a circulatory delivery issue of gases between the muscles and the lungs. An individual with a cardiac limitation may display a normal CPET pattern but with a lower than predicted $\dot{V}O_{2peak}$ and an early-onset AT. The typical performance-limiting symptom will be leg fatigue due to O_2 delivery failure and lactic acidosis at the tissue level, rather than dyspnoea. Patients may develop angina.

The key features are as follows (see Figure 8):

- Reduced $\dot{V}O_{2peak}$ to <80% predicted (relative to age, gender and height) with early-onset AT (plots 3, 6).
- HR may be increased during light exercise as the heart tries to increase its cardiac output without the ability to sufficiently recruit SV (plot 2).
- Peak HR commonly does not reach the age-predicted maximum due to impaired chronotropy from disease or b-blockade, causing a raised HRR (>15%).
- Normal linear increase in minute ventilation up to AT with no ventilatory limitation.
- A higher ventilatory equivalent for CO_2 can be a feature where LV failure may cause 'back up' or reduced pulmonary flow and worsening of VQ matching (plot 6).
- In severe disease, BP will either not increase normally with exercise or may even fall, requiring immediate abortion of the test.

Respiratory Limitation

Lung disease will result in exercise limitations due to ventilatory failure. Inadequate alveolar ventilation secondary to increased dead space, decreased tidal volumes and loss of alveolar volume causes low O_2 saturations and hypercapnia. With chronic obstructive pulmonary disease (COPD), progressive air trapping causes increased end-expiratory lung volume and extreme dyspnoea before the onset of an AT, which is often not achieved before terminating the test. With restrictive lung disease, the patient is much more reliant on respiratory rate to increase ventilation.

The key features are as follows (see Figure 9):

- Reduced $\dot{V}O_{2peak}$ –<80% predicted relative to age, gender and height (plot 3)
- Exhaustion due to ventilatory limitation prior to the onset of AT, so measurement is not achieved (plots 3, 5, 6)
- Elevated V_E for $\dot{V}O_2$ and $\dot{V}CO_2$ at all work rates (plot 6)
- Decreasing tidal volumes on increasing exercise secondary to air trapping in COPD or restriction in restrictive pathologies (plot 7)
- Low O_2 saturations due to VQ mismatch (plot 2)

Pulmonary Vascular Disease

Those with pulmonary vascular disease cannot increase pulmonary blood flow in response to a required rise in cardiac output. This means that as $\dot{V}_E$ increases with exercise, the dead-space fraction remains abnormally high as the individual ventilates areas of poorly perfused lung tissue. This causes a VQ mismatch. The elimination of CO_2 becomes inefficient. Patients tend to

	Cardiac	Ventilatory	Pulmonary Vascular Disease/ Interstitial Lung Disease
VO_{2peak}	Reduced	Reduced	Reduced
AT	Present (early)	Absent	Present (early)
$\dot{V}_E/\dot{V}CO_2$	May be increased	Increased	Increased
SpO_2	Stable	May decrease	May decrease
$pETCO_2$ (late exercise)	Decreased	Increased or Stable	Decreased
RER	Usually exceeds 1.1	Often remains below 1.0	Usually exceeds 1.1
Reason for premature termination	Leg fatigue	Dyspnoea	Dyspnoea, leg fatigue

Table. Summary of the Key Differences in CPET Parameters for the 3 Predominant Patterns of Limitation. Adapted from Luks et al.[7]

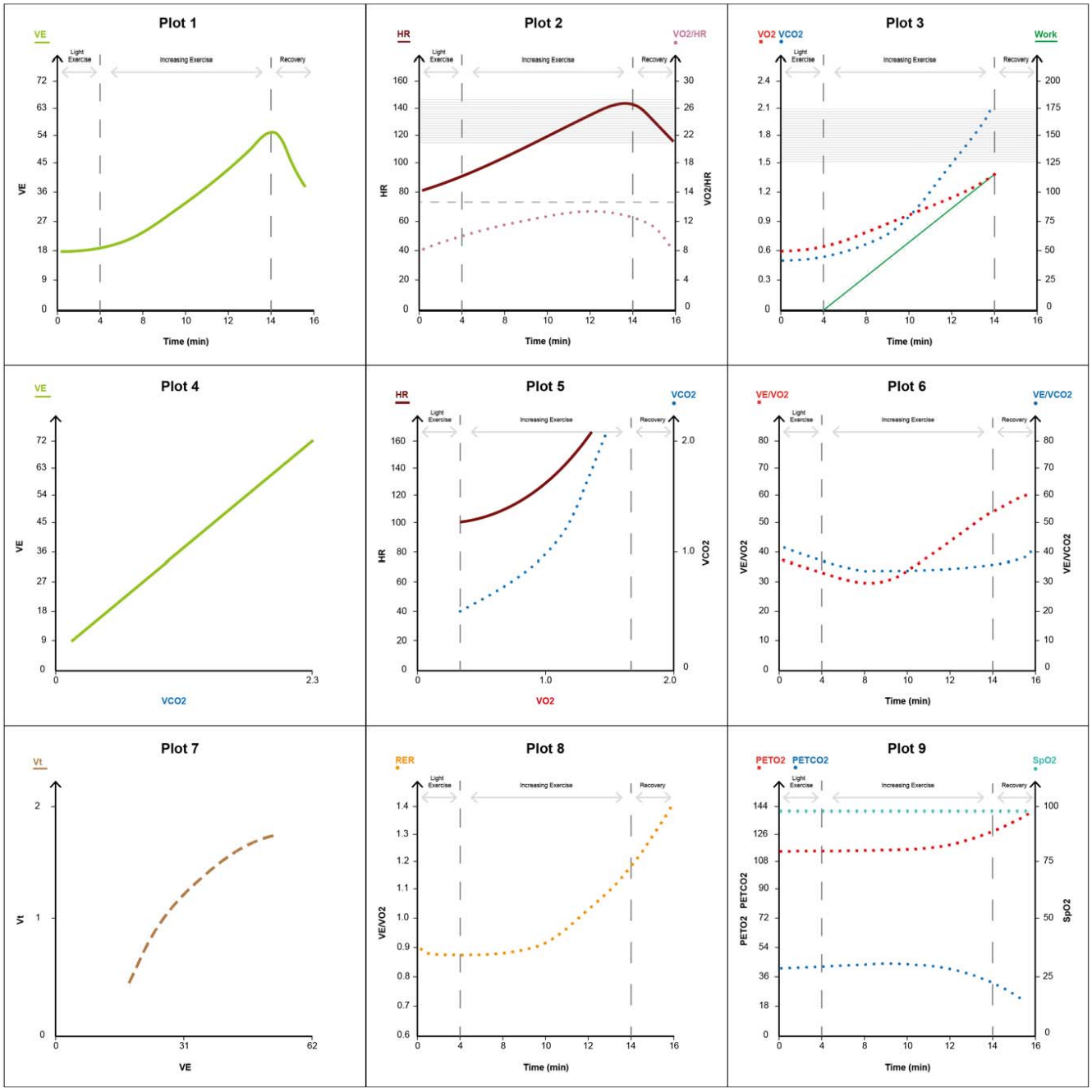

Figure 8. Cardiac limitation pattern.

have a low alveolar partial pressure of CO_2 ($PACO_2$) and partial pressure of end-tidal CO_2 ($pEtCO_2$), which decreases further with exercise. (Normally, in the absence of pulmonary vascular disease, the $\dot{V}_E/\dot{V}CO_2$ falls in the first stages of exercise as the VQ matching improves with better lung perfusion.) An echocardiogram is often subsequently requested to evaluate right heart pressures.

The key features are the following (see Figure 10):

- Reduced $\dot{V}O_{2peak}$ to <80% predicted, relative to age, gender and height (plot 3)
- Elevated HR disproportionate to work rate compared with normal individuals (plot 2)
- Desaturation with progressive exercise due to VQ mismatch (SpO_2 may be normal at rest; plot 9)
- Low $pEtCO_2$, which falls with exercise (plot 9)

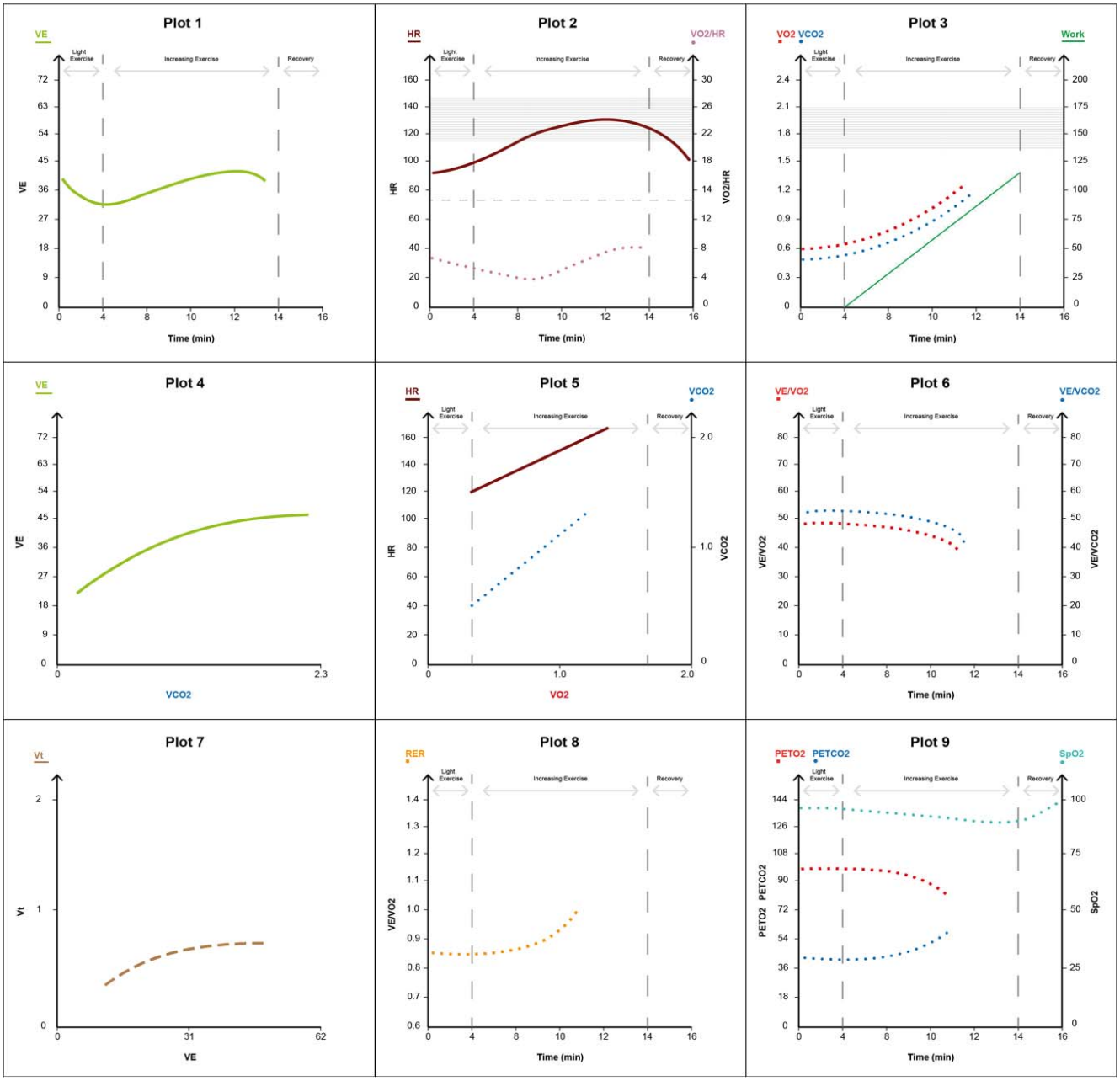

Figure 9. Respiratory limitation pattern.

- High $\dot{V}_E/\dot{V}CO_2$, which rises with unloaded cycling and continues to rise throughout the test due to increased dead space (plot 4)
- Early-onset AT (plots 3, 6)

APPLICATION OF CPET DATA

Studies evaluating the relationship between CPET performance and surgical outcome have found that $\dot{V}O_2$ peak, AT and $\dot{V}_E/\dot{V}CO_2$ are predictors of postoperative morbidity and mortality following noncardiac surgery.[8,9] The inability to complete the test, whether due to poor mobility, poor physiological reserve or inability to follow instructions, is also associated with an increased risk of postoperative morbidity and mortality.[10]

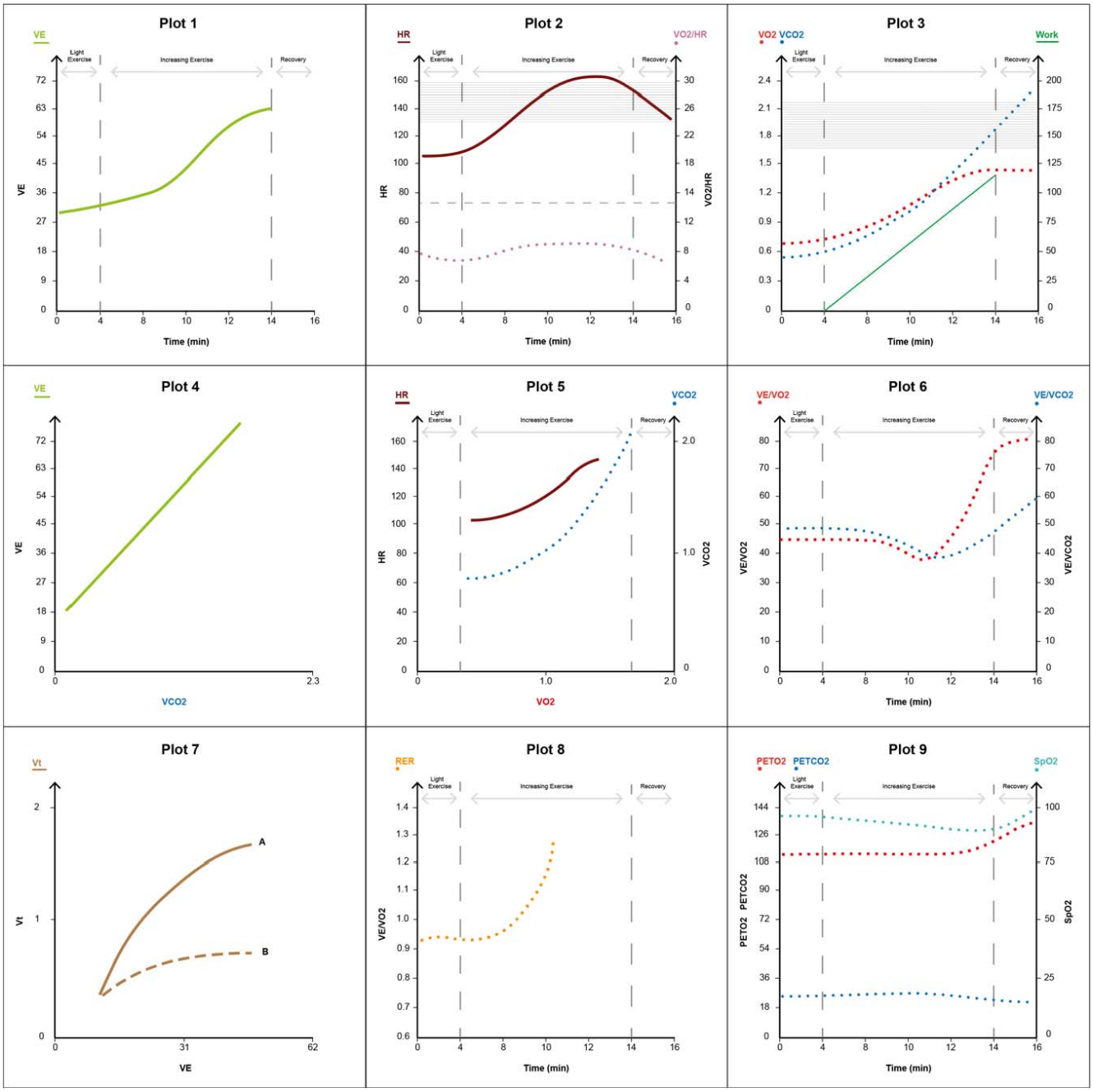

Figure 10. Pulmonary vascular disease pattern (plot 7: A, pulmonary vascular; B, interstitial lung disease).

Identified physiological limitations may trigger further investigation. For example, a patient with COPD may show a pattern in keeping with cardiac limitation of uncertain cause. An echocardiogram would be required to identify features such as valvular disease and ischaemic cardiomyopathy and for pulmonary artery pressure measurement.

In some centres, CPET data are being used to provide patients with focused prehabilitation programmes.[10]

Patients with CPET data showing significant limitation are identified as high risk. This raises an opportunity to discuss the risks and benefits of both surgical and nonsurgical options. Multidisciplinary discussion is prompted. The patient's ideas, concerns and expectations are understood, and a mutually agreed treatment plan is made.

Increasingly, CPET is being used to triage patients to intensive care, high-dependency or ward-based care for their postoperative management. A UK case-control study has shown that patients undergoing open colorectal surgery who are

assigned as 'high risk' with AT <11 mL·kg^{-1}·min^{-1} showed a significantly lower incidence of postoperative major cardiac events if they were managed in intensive care than those managed on a surgical ward.[11]

SUMMARY

In an era of an aging and increasingly comorbid population, CPET is a welcome tool that can be used to assist in the complex decision-making process faced by perioperative clinicians and their patients. In providing an objective summary of physiological reserve, it facilitates important discussions about an individual's perioperative care.

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