Perioperative cardiopulmonary exercise testing (CPET): consensus clinical guidelines on indications, organization, conduct, and physiological interpretation

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10 These authors contributed equally to the development of these guidelines.

Abstract

The use of perioperative cardiopulmonary exercise testing (CPET) to evaluate the risk of adverse perioperative events and inform the perioperative management of patients undergoing surgery has increased over the last decade. CPET provides an objective assessment of exercise capacity preoperatively and identifies the causes of exercise limitation. This information may be used to assist clinicians and patients in decisions about the most appropriate surgical and non-surgical management during the perioperative period. Information gained from CPET can be used to estimate the likelihood of perioperative morbidity and mortality, to inform the processes of multidisciplinary collaborative decision making and...
consensus, to triage patients for perioperative care (ward vs critical care), to direct preoperative interventions and optimization, to identify new comorbidities, to evaluate the effects of neoadjuvant cancer therapies, to guide prehabilitation and rehabilitation, and to guide intraoperative anaesthetic practice. With the rapid uptake of CPET, standardization is key to ensure valid, reproducible results that can inform clinical decision making. Recently, an international Perioperative Exercise Testing and Training Society has been established (POETTS www.poetts.co.uk) promoting the highest standards of care for patients undergoing exercise testing, training, or both in the perioperative setting. These clinical cardiopulmonary exercise testing guidelines have been developed by consensus by the Perioperative Exercise Testing and Training Society after systematic literature review. The guidelines have been endorsed by the Association of Respiratory Technology and Physiology (ARTP).

**Keywords:** anaerobic threshold; cardiopulmonary exercise testing; perioperative medicine

Use of preoperative cardiopulmonary exercise testing (CPET) to evaluate the risk of adverse perioperative events and inform the perioperative management of patients undergoing surgery has increased over the past decade, particularly in the UK.1–3 With the rapid uptake of CPET, standardization is key to ensure valid, reproducible results that can inform clinical decision making. Recently, an international Perioperative Exercise Testing and Training Society (POETTS) has been established (www.poetts.co.uk). This body developed from the UK National Perioperative CPET forum and has the specific aims of: (1) promoting the highest standards of care for patients undergoing exercise testing, exercise training, or both in the perioperative setting and to promote the professional practice of exercise testing, exercise training, or both in the perioperative setting; (2) promoting and delivering training and education in exercise testing, exercise training, or both in the perioperative setting including advising on education and training curricula for medical and healthcare practitioners; (3) promoting the development, conduct, and dissemination of audit, quality improvement, research and innovation to further the development of perioperative exercise testing, training, or both. These clinical cardiopulmonary exercise testing guidelines have been developed by consensus by the POETTS after systematic literature review. The guidelines have been endorsed by the Association of Respiratory Technology and Physiology (ARTP). The guidelines represent what is considered to be best practice by expert consensus and by setting a standard the intention is to help all who do perioperative CPET to reach this standard. They will be used to benchmark practice and subsequently will be revised in the light of new information or evidence.

**Methods**

**Guideline development**

An early set of UK CPET guidelines (unpublished) was produced by Helen Luery (University College London Hospitals, UK), Jonathan Wilson (York, UK), John Carlisle, and Michael Swart (Torbay, UK) in 2001, based on the work of Paul Older. The concept of consensus national guidelines was first formally raised at the first National Perioperative CPET Meeting at the Evidence Based Perioperative Medicine conference in July 2008 and formally discussed at the second meeting in 2009. Following initial open forum discussion at the third national CPET meeting in 2010, the authors produced the first draft of this manuscript based on systematic review of the literature (see below), guidelines from other applications of clinical CPET,1-3 established practice standards, and input from experts in the field (B.J. Whipp and others). The recommendations were reviewed by the authorship group until consensus was achieved by e-mail. The guidelines were then peer reviewed by the delegates at the National Perioperative CPET meetings. Firstly, an item-by-item chaired open discussion took place in 2011 and the document was revised and updated. Further point-by-point iterative discussion took place in chaired open discussion at the National CPET Meetings in 2012, 2013, 2014, and 2016. Consensus was achieved for elements without a firm evidence base. In this case, the recommendations are based on what is considered to be good practice standards by experts in the field. This final version was then refined and edited by the authors in late 2016 until all authors were satisfied with the final document which was then submitted for publication.

**Systematic review**

The writing process was informed by multiple published systematic reviews of the relevant literature including Smith and colleagues,6 Hennis and colleagues,7 and Moran and colleagues.8 In addition, to identify recently published studies, we performed repeated updated PubMed systematic searches during the development of this manuscript (until submission) based on the search strategy Hennis and Grocott7 and using the follow search terms: ‘CPET/surgery’, ‘CPEX/surgery’, ‘CFX/surgery’, ‘cardiopulmonary/exercise testing/surgery’, ‘VO2 peak/surgery’, ‘VO2max/surgery’ ‘AT/surgery and ‘Anaerobic threshold/surgery.’

**Strength of recommendations and levels of evidence**

To indicate the basis on which recommendations were made, all evidence was classified according to an accepted hierarchy of evidence that was originally adapted from the US Agency for Healthcare Policy and Research Classification.5 Each recommendation is graded A–D based on the level of associated evidence using a scheme formulated by the Clinical Outcomes Group of the NHS Executive that has been used in NICE guidelines9 (see Supplementary Appendix S1).

In contrast to questions of clinical efficacy and effectiveness, the practice recommendations within these guidelines relate to the indications, organization, conduct, and physiological interpretation of perioperative CPET. Such questions are rarely, if ever, amenable to direct evaluation through randomized controlled trials (RCTs); therefore, all recommendations are graded B (well-conducted clinical studies but no RCTs on the topic of recommendation or extrapolated from RCT or systematic review), C (expert committee reports or opinions/clinical experiences of respected authorities OR extrapolated from well-conducted clinical studies)—this grading indicates that directly applicable clinical studies of
good quality are absent or not readily available), or D (recommended good practice standard based on the clinical experience of the guidelines development group).

Guidelines scope
CPET evaluates the integrated physiological response to exercise and provides an objective measure of exercise capacity (functional capacity or physical fitness). It also permits interrogation of the etiology of exercise intolerance when exercise capacity is abnormal. Exercise capacity is predictive of postoperative outcome, reflecting the physiological reserve available to respond to the stress of surgery and postoperative recovery. This guideline is intended to provide guidance on the use of CPET perioperatively. The use of CPET for other applications has been comprehensively covered elsewhere.

Indications and contraindications for CPET
Indications
CPET is indicated to provide an objective assessment of exercise capacity preoperatively and to identify the causes of exercise limitation. This information may be used to assist clinicians and patients in decisions about the most appropriate surgical and non-surgical management during the perioperative period. Studies support the use of CPET for risk prediction in major abdominal surgery, colorectal surgery, urological surgery, hepatobiliary surgery, liver transplantation, bariatric surgery, vascular surgery, thoracic surgery, and oesophageal–gastric surgery, and also for guiding exercise-training interventions prior to surgery, immediately after surgery, or both. The evidence supporting CPET is continuously evolving and consequently the indications for CPET require regular reassessment.

Recommendations: Indications for CPET
(1) To estimate the likelihood of perioperative morbidity and mortality and contribute to preoperative risk assessment (Grade B).
(2) To inform the processes of multidisciplinary shared decision-making and consent (Grade C).
(3) To guide clinical decisions about the most appropriate level of perioperative care (ward vs critical care; Grade B).
(4) To direct pre-operative referrals/interventions to optimize comorbidities (Grade C).
(5) To identify previously unsuspected pathology (Grade B).
(6) To evaluate the effects of neoadjuvant cancer therapies including chemotherapy and radiotherapy (Grade B).
(7) To guide prehabilitation and rehabilitation training programmes (Grade B).
(8) To guide intraoperative anaesthetic practice (Grade D).

Contraindications for CPET
Published contraindications to CPET have addressed its use as a diagnostic and prognostic tool for patients with cardiac or respiratory disease, to monitor disease progression in chronic cardiorespiratory disease, to quantify exercise capacity, and to evaluate likely causes of exercise intolerance. These are largely based on the expert opinion of respected authorities.

Contraindications and relative contraindications to exercise testing in the perioperative setting are summarized in Table 1. These are based on recommendations in other areas of CPET modified for the perioperative context to take into account the specific patient population (Grade C). Patients with relative contraindications should be directly supervised by a physician (Grade C). For relative contraindications to exercise testing, the risks and potential benefits of undertaking CPET should be considered on a patient-by-patient basis both before and during the test (Grade D). If the risk-benefit relationship changes as the test progresses, the test can be terminated early—a submaximal test (Grade D). For example, in a colorectal cancer patient with newly identified asymptomatic severe aortic stenosis, CPET may be considered to delineate the functional impairment caused by the valve stenosis. The test may help determine the relative priority of valve replacement and tumour resection. However, if the patient developed chest pain or hypotension during the test, this would indicate critical stenosis and an increased risk of syncope, and should lead to test termination.

Perioperative CPET service structure and supervision
A perioperative CPET service should be managed and led by an individual expert in perioperative CPET (Grade C). Perioperative CPET expertise incorporates an understanding of the

<table>
<thead>
<tr>
<th>Absolute contraindications</th>
<th>Relative contraindications</th>
</tr>
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<tbody>
<tr>
<td>• Acute myocardial infarction (3–5 days)</td>
<td>• Untreated left main stem coronary stenosis</td>
</tr>
<tr>
<td>• Unstable angina</td>
<td>• Asymptomatic severe aortic stenosis</td>
</tr>
<tr>
<td>• Uncontrolled arrhythmia causing symptoms or haemodynamic compromise</td>
<td>• Severe untreated arterial hypertension at rest (&gt;200 mm Hg systolic, &gt;120 mm Hg diastolic)</td>
</tr>
<tr>
<td>• Syncope</td>
<td>• Tachyarrhythmias or bradyarrhythmias</td>
</tr>
<tr>
<td>• Active endocarditis</td>
<td>• Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>• Acute myocarditis or pericarditis</td>
<td>• Significant pulmonary hypertension</td>
</tr>
<tr>
<td>• Symptomatic severe aortic stenosis</td>
<td>• Thrombosis of the lower extremity until treated for a minimum of 2 weeks</td>
</tr>
<tr>
<td>• Uncontrolled heart failure</td>
<td>• Within 2 weeks of acute symptomatic pulmonary embolus</td>
</tr>
<tr>
<td>• Suspected dissecting or leaking aortic aneurysm</td>
<td>• Abdominal aortic aneurysm &gt;8.0 cm</td>
</tr>
<tr>
<td>• Uncontrolled asthma</td>
<td>• Electrolyte abnormalities</td>
</tr>
<tr>
<td>• Arterial desaturation at rest on room air &lt;85%</td>
<td>• Advanced or complicated pregnancy</td>
</tr>
</tbody>
</table>
equipment and exercise protocols, expertise in exercise physiology and pathophysiology and an understanding of perioperative risk.

Perioperative CPET testing and interpretation can be divided into three distinct stages. **Stage 1, CPET practitioner:** the practicalities of test performance, including the exercise protocol, equipment operation and maintenance and quality control. **Stage 2, Advanced CPET practitioner:** integration of the physiological data to provide a comprehensive interpretation of the patient’s exercise capacity and the main causes of exercise limitation, including the identification of undiagnosed pathology. **Stage 3, CPET competent perioperative physician:** interpretation of the implications of the patient’s exercise limitation for their perioperative risk and formulating recommendations for preoperative interventions and perioperative care.

The competencies required for each of these stages are different. Within a CPET service different individuals may perform each of the three stages of the testing and interpretation process. Alternatively, a single individual may be able to perform all three stages. Stages 1 and 2 may be performed by non-clinicians, but clinical expertise in perioperative medicine is required for stage three. Competence and expertise in each stage of the CPET process should be defined by specific training and documented experience, rather than defined medical roles (e.g. doctor, nurse, clinical physiologist; Grade C).5

All competent CPET practitioners and advanced practitioners must be able to identify and manage adverse events in relation to CPET by discriminating between normal and abnormal responses to exercise including abnormal symptoms, hypotension, hypotension, abnormal arterial O₂ saturation [measured by pulse oximetry (SpO₂)] and ECG evidence of arrhythmia and ischaemia (Grade C).5 CPET practitioners and advanced practitioners must have appropriate knowledge and experience in first aid and resuscitation (Grade C).5

A minimum of two members of staff should be directly available for every test, one of whom should be a competent CPET advanced practitioner (Grade D). At least one member of staff should have current intermediate life support competence and the other a minimum of current basic life support with automated external defibrillator competence (defined by Resuscitation Council UK criteria, www.resus.org.uk; Grade Q).5 A resuscitation team with advanced life support skills (cardiac arrest team or paramedic team) must be immediately available (Grade Q).5 A physician should be available to review any patient who develops complications during a test (Grade Q).5 High-risk CPET tests, including tests where relative contraindications are present (Table 1), should be directly supervised by a physician (Grade Q).5

When a new service is being set up without established local expertise, formal mentoring from a suitably accredited trainer is recommended (e.g. POETTS accreditation; Grade D). CPET practitioners who will be performing and reporting perioperative CPET tests should have completed an accredited course, performed 25 tests under supervision, and reported at least 50 tests under supervision before gaining accreditation and reporting independently (Grade Q).5 CPET practitioners should review or report 25 tests per year to maintain their competence (Grade C).5 CPET practitioners who will be performing CPET tests but not interpreting tests should complete an accredited course and perform a minimum of 25 tests under supervision before testing independently (Grade D).

**Preparation for the exercise test (Grade C, good practice recommendations, unless otherwise stated)**

**Patient information and consent**

Patients should be provided with information on the process, risks, and benefits of CPET. The process of informed decision-making and consent should be documented and may involve formal written consent. Patients should take their regular medication but avoid caffeine, alcohol, cigarettes, and strenuous exercise on the day of testing. For 2 h prior to the test, patients should not eat and should drink only water.

**Risk of adverse events**

CPET is a relatively safe investigation, especially in individuals with no comorbidity. A review of the exercise testing literature (primarily in patients with cardiac disease), suggests an incidence of a complication requiring hospitalization of two or less in 1000,5 of a major cardiac event of 1.2 per 10,000 tests,13,35 and of mortality of two to five per 100,000 clinical exercise tests.3,5 To date, no deaths have been reported during perioperative CPET in the UK.

**Baseline data collection**

Baseline data collection should include patient demographic information, the reason for referral and the proposed surgery.5 The patient's medical history should be reviewed with particular attention to cardiac and respiratory disease to identify potential contraindications to exercise testing.7 A full drug history should also be taken to identify medication that may interfere with the exercise response.5 A recent haemoglobin level should be reviewed, since anaemia may impair exercise capacity (Grade D).36,37

**Conduct of the exercise test (Grade C, good practice recommendations, unless otherwise stated)**

The exercise protocol, equipment, and quality control of perioperative CPET are discussed below. The recommendations within this section are based on key position statements and policy documents from national and international specialist bodies that use CPET in other clinical contexts and represent good practice standards.3–5,12,13

**Exercise protocol (Grade C)**

Cardiopulmonary exercise testing provides a global assessment of the integrated response of the pulmonary, cardiovascular, metabolic, and haematological systems. Key is the integration of expired gas analysis (O₂ and CO₂ concentrations) with ventilatory flow measurements, thereby enabling calculation of O₂ uptake (VO₂) and CO₂ output (VCO₂), typically on a breath-by-breath basis, under conditions of progressively increasing physiological stress imposed by a defined profile of external work rate (WR).

Heart rate (HR), SpO₂, arterial blood pressure, and 12-lead ECG (for rate, rhythm, and S-T segment morphology evaluation) should be monitored throughout the test.3–5,12,13 Resuscitation equipment including supplemental O₂ must be immediately accessible.3–5,12,13
For perioperative CPET, the rapid ramp (or incremental) exercise test performed to the limit of tolerance should be used.\textsuperscript{38} The advantages of this protocol are as follows: (1) it evaluates the exercise response across the entire range of functional capacity; (2) the initial WR is low and there is a relatively short duration of high intensity exercise; (3) the entire protocol is of short duration, with 8–12 min of exercise during the incremental phase; (4) it permits assessment of the normality or otherwise of the exercise response; (5) it permits identification of the cause of functional exercise limitation; and (6) it gives an appropriate frame of reference for training or rehabilitation targets.

Submaximal tests, (stopping the incremental ramp above the anaerobic threshold but before peak exercise) were initially widely used in the perioperative setting, primarily because of safety concerns and may still be considered in some clinical contexts, for example, in patients with angina or moderate to severe aortic stenosis. However, maximal tests to the limit of tolerance provide additional information that may have prognostic and diagnostic utility and are preferred.

Cycle ergometry has been used in all bar one of the published perioperative CPET cohorts. Cycle ergometry permits accurate determination of the external WR and thus, for example, evaluation of the VO\textsubscript{2}–WR relationship, which is difficult with a treadmill.\textsuperscript{39} Consequently, cycle ergometry (using an electromagnetically braked ergometer) is the preferred mode of exercise for PCPET. For patients who are unable to perform cycle ergometry, arm cranking may be considered, although the risk thresholds for this mode of exercise in the perioperative setting have not been identified.\textsuperscript{40}

A period of approximately 3 min of resting data collection (rest phase) should be followed by 3 min of resistance-free pedalling (unloaded cycling phase) and then a continuous gradual, uniform increase in WR until the limit of tolerance is attained (incremental phase). The ramp slope (W min\textsuperscript{-1}) is selected to produce 8–12 min of exercise during the ramp phase.\textsuperscript{3} For healthy active individuals, ramp slopes of 15, 20, or 25 W min\textsuperscript{-1} are common, while lower values in the range of 5–15 W min\textsuperscript{-1} are more appropriate for most patients. Higher ramp slopes in frail patients are likely to lead to premature test termination and consequently a truncated period of data acquisition, which precludes reliable test interpretation. Algorithms based on individual patient characteristics (age, height, weight) are available to estimate the ramp slope required to produce a test duration of approximately 10 minutes (i.e. within the recommended 8–12 min range). For example:\textsuperscript{41}

\[
\text{ramp slope (W min}^{-1}) = \frac{\text{VO}_{2\text{peak}} - \text{VO}_{2\text{unloaded}}}{100}
\]

where:

\[
\text{VO}_{2\text{unloaded}} (\text{ml min}^{-1}) = 150 + [6 \times \text{weight (kg)}]
\]

and for males:

\[
\text{VO}_{2\text{peak}} (\text{ml min}^{-1}) = [\text{height (cm)} - \text{age (yr)}] \times 20 f
\]

or for females:

\[
\text{VO}_{2\text{peak}} (\text{ml min}^{-1}) = [\text{height (cm)} - \text{age (yr)}] \times 14
\]

The validity of such predictive algorithms in a general surgical population has not been established.\textsuperscript{42} Anecdotal evidence suggests that exercise capacity of the surgical patient population tends to be overestimated by these equations; a reduction in the calculated value should therefore be considered (Grade D).

**CPET equipment (Grade C)**

Test equipment should include an electronically-braked cycle ergometer and a metabolic cart capable of analyzing respired flow, [O\textsubscript{2}], and [CO\textsubscript{2}] with a response time <90 ms to provide breath-by-breath measurements of ventilatory and gas exchange variables, together with ancillary equipment for serial monitoring of Sp\textsubscript{O2}, blood pressure, ECG, and perceptual responses (perceived exertion, dyspnoea).\textsuperscript{3,4,15,39} Perceptual responses such as perceived exertion and breathlessness can be assessed by the Borg scale or a visual analogue scale.\textsuperscript{43,44}

**Calibration and quality control (Grade C)**

The accuracy and reproducibility of the values obtained during testing is dependent on meticulous quality control.\textsuperscript{3,4,15,39} Calibration of primary sensors for flow and O\textsubscript{2} and CO\textsubscript{2} gas measurement should be performed immediately before each exercise test. The calibration should consider barometric pressure, ambient humidity, and temperature. While the precise calibration procedures will vary with the model and manufacturer of the metabolic cart, there are certain underlying principles that should be followed.

The flow sensor should be calibrated for volume with a precision syringe (typically 3 l) over a physiological range of flow rates. Calibration gas mixtures for the O\textsubscript{2} and CO\textsubscript{2} sensors should be prepared by gravimetric weighing to ensure a concentration accuracy of ±1%. Sensor calibration should be performed at two points, within the range for inhaled (21% O\textsubscript{2} and 0% CO\textsubscript{2} in N\textsubscript{2}) and exhaled gas compositions (e.g. 15% O\textsubscript{2} and 5% CO\textsubscript{2} in N\textsubscript{2}). Because of the transport delay associated with the gas concentration sensors (a phase delay typically in the region of 250 ms), the flow and gas concentration signals have to be time-aligned prior to further processing. This phase delay should be measured prior to each test rather than assumed, as small deviations from the correct value can have significant impact on gas exchange computations.\textsuperscript{4,15,29,39,45} It is measured as the delay between the imposition of a step change in gas concentration at the distal end of the sample line and the resulting gas concentration response at the respective sensor (phase delay), and values should lie within the manufacturer’s stated range.

The performance of the gas exchange algorithms cannot be assessed in the routine pretest calibration phase. This requires simultaneous comparison of the metabolic cart responses with those obtained with an accepted independent standard. The contemporary (and expensive) ‘gold standard’ method uses an automated gas exchange simulator. This comprises a reciprocating piston system that generates ‘expired’ gas to simulate metabolic rates by injecting a precision gas mixture into a chamber at precisely metered rates to mix with inspired air, thus allowing comparison of ‘measured’ breath-by-breath values of VO\textsubscript{2}, VCO\textsubscript{2}, and ventilation (VE) with predicted values.\textsuperscript{46} It has been proposed that the measured outputs and their variation with changes in pump frequency should lie within ±5%. Values falling outside this range should prompt a comprehensive reassessment of the entire monitoring system.\textsuperscript{47} Small, progressive deteriorations in sensor performance and sample line transit delay over time may have a significant effect on gas exchange computation. Validation against a gas
exchange simulator may be performed annually as part of the metabolic cart service.

A practical (and inexpensive) alternative is provided by regular ‘biological quality control’ (conducted monthly or more frequently), utilizing responses of a ‘standard’ subject (typically a member of the laboratory staff familiar with testing procedures). It is recommended that the subject performs two sub-anaerobic threshold (AT) constant WR tests, each of at least 6 min duration, with the steady-state VO$_2$, VCO$_2$, and VE responses at each WR being obtained by averaging data over the final 2 min of the test (i.e. when a steady state has been achieved; Fig. 1). This allows the development of a serial quality control database comprising absolute VO$_2$, VCO$_2$, and VE responses at standardized WRs, as well as derived indices such as the respiratory exchange ratio (RER, VCO$_2$/VO$_2$) and the slope of the VO$_2$−WR relationship (ΔVO$_2$/ΔWR), which is relatively independent of age, gender, and fitness. Differences in ‘expected’ response can then be identified, both in terms of previous subject performance and also relative to normal population values. While there are no formal recommendations for assigning a ‘significant’ change relative to a quality control database, decisions could be based on: (1) responses falling outside the database 95% confidence interval; (2) VO$_2$ at a given WR deviating by >5–10% of database values or >10% of the predicted value, where VO$_2$ pred = [5.8 × weight (kg)] + 151 + (10.1 × W)$^{35}$; or (c) ΔVO$_2$/ΔWR between the two WRs deviating (above or below) from database values or from a normal of −10–11 ml min$^{-1}$ W$^{-1}$, with 95% CI −8.5–12.5 ml min$^{-1}$ W$^{-1}$ 51–53.

Ideally, the cycle ergometer should be calibrated at least annually and whenever it is moved (which can disturb the calibration), using a device such as a dynamic torque meter. The calibration should be linear from 0 to −400 watts, and independent of pedalling cadence over a physiologically reasonable range.54–56 Sudden deviations in the normal slope value of the VO$_2$−WR relationship warrant investigation, both of cycle ergometer and metabolic cart performance.

### Practicalities of test conduct (Grade C)

Resting spirometry should be performed to measure forced vital capacity and forced expiratory volume in 1 s (FEV$_1$).

Maximum voluntary ventilation can be estimated from FEV$_1$ as (FEV$_1$ × 35) or (FEV$_1$ × 40). The patient should be familiarized with the cycle ergometer and the breathing assembly (facemask or breathing valve and mouthpiece), and should be instructed to give their ‘best effort’ but counselled to stop if symptoms such as chest pain develop. The patient should be discouraged from talking during the test, as this will compromise data quality; an alternative method of communication should be established before commencing the test (thumb up = yes, thumb down = no). The patient should understand that they can stop at any time, whilst recognizing that the aim is to pedal for as long as possible. During testing, data should be displayed in both tabular and graphical formats to monitor for abnormalities; core variables are presented in Table 2.

The exercise test consists of four main phases: rest, unloaded cycling, ramp exercise, and recovery.

#### Rest (3 min)

A minimum of 3 min of resting data should be recorded, with the ECG being monitored for ischaemia or arrhythmia. If hyperventilation is present (RER > 1.0) this should be allowed to settle before commencing the next phase of the test. It is important to note that sustained hyperventilation can precipitate a premature ‘false positive’ or ‘pseudothreshold’ for AT estimation, which can obscure events triggered by the actual threshold (see False positives below). Also, if the RER is persistently <0.7, the test should be halted as this is suggestive of inaccurate calibration and the calibration procedure should be repeated.

#### Unloaded cycling (3 min)

Unloaded cycling allows functionally limited patients to accimate to pedalling. Three minutes is sufficient in healthy individuals for HR, VO$_2$, VCO$_2$, and VE to attain new steady states prior to the ramp phase commencing. The patient is encouraged to adopt a comfortable pedalling cadence, between 55 and 75 rpm throughout the test.

#### Ramp phase (8–12 min)

It is recommended that this phase is started without providing any cues to the patient, who should be instructed to continue pedalling for as long as possible. The limit of tolerance is defined as the point at which the patient is unable to maintain the pedalling cadence despite encouragement. The Borg score may be recorded at the end of the exercise to evaluate subjective effort.

#### Recovery (~5 min)

Once the load is removed, the patient should be encouraged to pedal for a further period to prevent venous pooling in the legs and consequent syncope. Monitoring should continue until any dysrhythmia or ST changes have reverted to baseline, HR has fallen to within 10 beats min$^{-1}$ of resting values and blood pressure has returned to baseline.

### Indications for stopping the test (Grade C)

An exercise test may be terminated as a result of ostensive ‘good effort’ (i.e. with symptom limitation) or because of the development of clinically-inappropriate symptoms. The
Table 2 Key response variables reported for perioperative cardiopulmonary exercise testing

<table>
<thead>
<tr>
<th>Exercise capacity variables</th>
<th>Cardiorespiratory variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Anaerobic threshold (AT) (ml min⁻¹ and ml kg⁻¹ min⁻¹)</td>
<td>- VO₂-work rate slope (ΔVO₂/JWR) (ml min⁻¹ W⁻¹)</td>
</tr>
<tr>
<td>- Peak VO₂ uptake (VO₂peak) (ml min⁻¹ and ml kg⁻¹ min⁻¹)</td>
<td>- Heart rate (HR) (beats min⁻¹)—resting and peak exercise</td>
</tr>
<tr>
<td>- Peak work rate (WRpeak) (W)</td>
<td>- Heart rate reserve (HRR) (beats min⁻¹)—peak exercise = maximum predicted heart rate—measured maximum heart rate</td>
</tr>
</tbody>
</table>

Table 3 Indications for the premature termination of an exercise test (adapted from American Thoracic Society)³⁴

<table>
<thead>
<tr>
<th>Indication</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>&gt;2 mm ST depression if symptomatic or 4 mm if asymptomatic or &gt;1 mm ST elevation</td>
</tr>
<tr>
<td></td>
<td>Significant arrhythmias causing symptoms or haemodynamic compromise</td>
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<tr>
<td></td>
<td>Fall in systolic blood pressure &gt;20 mm Hg from the highest value during the test</td>
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<tr>
<td></td>
<td>Hypertension &gt;250 mm Hg systolic; &gt;120 mm Hg diastolic</td>
</tr>
<tr>
<td></td>
<td>Severe desaturation: SpO₂ &lt;80% (lower may be accepted in patients with known underlying lung disease)</td>
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<tr>
<td></td>
<td>Loss of coordination</td>
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<tr>
<td></td>
<td>Mental confusion</td>
</tr>
<tr>
<td></td>
<td>Dizziness or faintness</td>
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</table>

Table 4 Key elements in preoperative cardiopulmonary exercise testing interpretation

1. Determine the reason for cardiopulmonary exercise testing
2. Review pertinent medical history and laboratory information
3. Note overall test quality, assessment of patient effort and reasons for test termination
4. Use tabular and graphical presentation of the data
5. Report exercise capacity using anaerobic threshold and VO₂peak values
6. Report other indices related to perioperative risk e.g., VE/VO₂ at the anaerobic threshold
7. Evaluate exercise limitation and primary cause(s) for this, e.g., cardiovascular, respiratory, deconditioning
8. Comment on perioperative risk implications of the exercise test and suggestions for further investigation/referral/preoperative interventions

Interpretation of the exercise test

Interpretation of a PCPET includes two main elements: (1) integration and interpretation of the physiological data to provide a comprehensive description of the patient’s exercise capacity and the main causes of exercise limitation. (Table 4); and (2) interpretation of the implications of the patient’s exercise limitation for their perioperative risk and recommendations regarding preoperative interventions (beyond the scope of this guideline; to be addressed in a subsequent guideline).

While the former can be standardized, the latter is based on incorporation of functional capacity into the overall patient preoperative assessment. The latter is an evolving field with a requirement for frequent (re-)evaluation of the clinical literature and will be the subject of a later guideline. In this guideline we focus on the interpretation of exercise capacity, which is a fundamental consideration in perioperative risk evaluation. We will also discuss the ventilatory equivalents for CO₂ as this is associated with surgical outcome in several surgical cohorts.¹⁷,²⁶ It is likely that as the field develops other variables may be related to outcome and these guidelines will be reviewed and revised as appropriate. Detailed interpretation of underlying cardiac and respiratory patholology is covered elsewhere.²⁻⁵,¹²⁻¹⁵ An integrated approach to perioperative CPET interpretation and the key elements of a perioperative CPET report are also considered.

Data averaging and data presentation (Grade C, good practice recommendations, unless otherwise stated)

The breath-by-breath data should be averaged prior to graphical display and interpretation using, for example, a moving average (e.g. middle five of seven breaths), a breath-based average (e.g. three to five breaths), or a time-based average (e.g. ~20 s), to reduce the influence of biological ‘noise’.⁶⁰,⁶¹

The procedures for data editing and data averaging should be applied consistently within a CPET laboratory; otherwise, results may be adversely influenced.⁶²,⁶³ The quality of the test should also be commented upon in the report.
Key exercise response variables and their physiological basis

The key response variables typically recorded during the CPET test are summarized in Table 2. A comprehensive description of these variables may also be found in key position statements and policy documents.3–5,12,13

Reporting exercise capacity or functional capacity (Grade C, good practice recommendations, unless otherwise stated)

The terms functional capacity, exercise capacity, and exercise tolerance are used synonymously to describe the patient’s ability to perform exercise and thus provide insight into his/her physiological reserve. Two variables are widely used to describe exercise capacity in perioperative CPET: VO2peak and the AT. These variables are both associated with postoperative morbidity and mortality.8

VO2peak (see Table 5 for summary)

VO2peak is a metabolic rate defined as the highest oxygen uptake (VO2) attained on a rapid incremental test at end-exercise. As such, it is reflective of the patient’s ‘best effort’ but it may not reflect what was potentially achievable for that patient (i.e. it is not necessarily a physiologically maximal end-point).

The highest VO2 that could be attained by a patient is defined as the maximum VO2 (VO2max) ‘the oxygen uptake during an exercise intensity at which actual oxygen uptake reaches a maximum beyond which no increase in effort can raise it’ (a physiological end point).64 Rigorous determination of VO2max relies on demonstration of a plateau in VO2 in the face of increasing WR, e.g. VO2 increasing by <2 ml kg\(^{-1}\) min\(^{-1}\) (or 50% of the predicted increase over 1 minute). The classical approach for determining VO2max is demanding as it requires the completion of several discrete exhausting constant WR tests.66,67 VO2max reflects the attainment of a physiological limitation at one or more points in the O2 transport pathway between the lungs and the site of the mitochondrial O2 consumption at the cytochrome oxidase terminus of the electron transport chain.68 Thus, dysfunction in the responses of the convective pulmonary or vascular O2 fluxes, or in the diffusive pulmonary or muscle-tissue O2 fluxes will result in an abnormally low VO2max.

VO2peak may reflect the patient’s physiological limits but this can only be assumed if there is a plateauing of the VO2–WR relationship as the limit of tolerance is approached.69 Unfortunately not all individuals will exhibit a plateau during rapid incremental exercise even when they have attained a physiological maximum.70,71 In the absence of a plateau in the VO2 response, additional criteria may be used to help support VO2peak representing a physiologically maximal effort, including a peak HR within 10 beats min\(^{-1}\) of the age-predicted maximum and a peak RER of >1.1.72 It should be noted, however, that pathology or medication may affect either or both of these criteria in a patient population, for example, chronotropic incompetence or β-blockade reducing the maximum HR response or respiratory-mechanical flow limitation limiting exercise before the generation of a metabolic acidosis in severe chronic obstructive pulmonary disease resulting in a peak RER < 1. Thus, an effort may be physiologically maximal without these criteria being attained and consequently they should be interpreted with caution in the light of the entire exercise response. Furthermore, VO2peak may be affected by the patient’s volitional exercise effort.72

Despite the uncertainty regarding the presence of physiological limitation at VO2peak, importantly VO2peak has been shown to predict both postoperative morbidity and mortality in surgical populations and so has predictive clinical utility.71 In addition, it is both easy to identify and reproducible. A good patient effort is aided by familiarization prior to the test as well as encouragement by the investigator during the later stages of the test.

VO2peak should be calculated as an averaged value over a short period extending from the end-exercise point back into the incremental phase to minimize the influence of breath-to-breath noise, i.e. capturing the true end-point without weighting it unduly towards submaximal breath values.63,74 A reasonable choice is a period of ~20 s or ~three to five breaths, with the value being reported, as an absolute value (ml min\(^{-1}\) or litres min\(^{-1}\)) or indexed to bodyweight (ml kg\(^{-1}\) min\(^{-1}\)). With good subject effort, VO2peak is independent of the WR incrementation rate.75 However, this is not the case for peak WR, which is progressively greater the faster the rate of WR increase (i.e. the greater the incremental ramp gradient) because of the underlying VO2 response kinetics.75 As a consequence, peak WR varies with the ramp gradient and consequently is not as reproducible as VO2peak.

In summary, VO2peak is a measure of maximal exercise capacity but may be affected by volition. Practically, VO2peak is easy to identify and reproducible. Importantly, it predicts postoperative outcome in major surgical patients.

Anaerobic Threshold (AT) (Table 6 for summary)

The AT provides an index of submaximal, sustainable exercise capacity, and if present cannot be volitionally influenced by the patient. Importantly, it predicts postoperative complications and mortality in a wide range of surgical populations with more precision than other CPET variables.11

The AT is a metabolic rate defined as the VO2 above which arterial [lactate] first begins to increase systematically during incremental exercise.96 The lactate accumulates as a

<table>
<thead>
<tr>
<th>Table 5 VO2peak definition, identification and key characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2peak Definition, Measurement, and Key Characteristics</td>
</tr>
<tr>
<td>VO2peak is a metabolic rate defined as the highest VO2</td>
</tr>
<tr>
<td>attained on a rapid incremental test at end-exercise</td>
</tr>
<tr>
<td>VO2peak should be calculated as an averaged value over</td>
</tr>
<tr>
<td>~20 s or ~three to five breaths</td>
</tr>
<tr>
<td>VO2peak should be reported as an absolute value (ml min(^{-1})</td>
</tr>
<tr>
<td>or litres min(^{-1}) and indexed to bodyweight (ml kg(^{-1})</td>
</tr>
<tr>
<td>min(^{-1}))</td>
</tr>
<tr>
<td>VO2peak is reproducible and is independent of the ramp</td>
</tr>
<tr>
<td>gradient</td>
</tr>
<tr>
<td>VO2peak may be affected by patient volition</td>
</tr>
<tr>
<td>VO2peak is associated with post-operative morbidity and</td>
</tr>
<tr>
<td>mortality in the majority of clinical cohorts</td>
</tr>
</tbody>
</table>
consequence of anaerobic glycolysis and its associated metabolic acidosis. However, the causes of this remain controversial. The AT may also be termed the lactate threshold, lactic acidosis threshold, ventilatory threshold, or gas exchange threshold. In the perioperative CPET literature, the term anaerobic threshold has been used consistently and is consequently preferred (Grade D). The AT is conventionally estimated non-invasively from respired gas measurements using an incremental ramp exercise test. The AT should be identified using a three-criterion discrimination technique as described by Whipp and colleagues. The modified V-slope method can be used to identify the inflection point in the CO2 output (VCO2) response and this should be supported by evaluating changes in the ventilatory equivalents and end-tidal partial pressures of O2 and CO2 to confirm hyperventilation with respect to oxygen but not to carbon dioxide. The methods used to identify the AT are summarized in Table 6.

**Table 6** Anaerobic threshold (AT) definition, measurement and key characteristics

<table>
<thead>
<tr>
<th>AT—definition, identification, and key characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>The AT is a metabolic rate expressed in ml kg⁻¹ min⁻¹ or ml min⁻¹. It is defined as the VO₂ above which arterial (lactate) first begins to increase systematically during incremental exercise reflecting increased glycolysis.</td>
</tr>
<tr>
<td>The AT should be identified using a three-criterion discrimination technique (Fig. 4)</td>
</tr>
<tr>
<td><strong>AT Criterion 1:</strong> identify excess VCO₂ relative to VO₂ above the AT by:</td>
</tr>
<tr>
<td>• Modified V-slope: (Fig. 3) The tangential breakpoint in the VCO₂ – VO₂ relationship identified as the intersection point of one ‘line of one’ (ΔVCO₂/ΔVO₂ = 1.0) and the baseline. The inflection point is identified by moving the line of one from the right until it first impacts on the VCO₂–VO₂ relationship. The VO₂ at which this occurs is taken as the AT.</td>
</tr>
<tr>
<td>• V-slope: (Fig. 2) The inflection point in the VCO₂–VO₂ relationship identified as the intersection point of the linear regression lines of the S1 (below AT) and S2 (above AT) components. The initial kinetic portion of the relationship and the portion above the respiratory compensation point are excluded from the linear regression.</td>
</tr>
<tr>
<td><strong>AT Criterion 2:</strong> identify hyperventilation relative to oxygen (Fig. 4)</td>
</tr>
<tr>
<td>• The VE/VO₂–VO₂ relationship having been flat or decreasing begins to increase and does not return to baseline.</td>
</tr>
<tr>
<td>• The PₚO₂–VO₂ relationship having been declining or flat begins to increase and does not return to the baseline.</td>
</tr>
<tr>
<td><strong>AT Criterion 3:</strong> exclude hyperventilation relative to CO₂ (Fig. 4) at the AT inflection point identified by criteria 1 and 2:</td>
</tr>
<tr>
<td>• The VE/VCO₂ relationship remains constant or continues to decrease at the point where VE/VO₂ starts to rise systematically.</td>
</tr>
<tr>
<td>• There is no reciprocal decrease in PETCO₂ at the point where PETCO₂ starts to rise systematically.</td>
</tr>
</tbody>
</table>

**AT Criterion 1:** Excess VCO₂ above the AT is identified using the V-Slope method:

The increasing anaerobic glycolysis above the AT results in a progressive metabolic acidosis. This is buffered to an extent by intra- and extracellular bicarbonate [HCO₃⁻] in the exercising muscle. Consequently, arterial [HCO₃⁻] starts to decrease as WR increases above the AT, essentially mirroring the developing [lactate] increase. These buffering reactions generate CO₂ that is additional to the CO₂ produced during aerobic metabolism (i.e. ‘excess’ VCO₂). Thus VCO₂ is supplemented and the VCO₂–VO₂ relationship steepens at the AT causing an inflection in the VCO₂–VO₂ response. The AT is identified by this inflection point in the VCO₂–VO₂ response and can be detected by the V-slope method (Fig. 2) or by the modified V-slope method (Fig. 3). This inflection point has been demonstrated to coincide with the first point of systematic increase in arterial [lactate] and decrease in arterial [HCO₃⁻] and thus does not originate in either an acceleration of aerobic metabolism or in acute hyperventilation relative to CO₂.

**V-slope method** (Fig. 2). At the start of the incremental phase of the test, the VO₂ response initially lags behind that of VCO₂ reflecting its slower response kinetics. The VCO₂ then increases linearly with respect to VO₂. The slope of the VCO₂–VO₂ relationship (ΔVCO₂/ΔVO₂) in this linear region has been termed S₁ and has a value typically slightly less than one in patients on a typical western diet (i.e. reflecting the influence of the respiratory quotient). Immediately above the AT, the gradient of the VCO₂ – VO₂ relationship becomes steeper as excess VCO₂ develops, with a slope termed S₂. The AT is the point at which the linear regression lines of the S1 and S2 components intersect (the S₁–S₂ inflection point). The initial portion of the VCO₂ – VO₂ relationship that is distorted by changes in body CO₂ stores—the ‘kinetic’ phase (approximately the first 60 s exercise) and the portion of the curve above the respiratory compensation point (RCP; defined as >15% change in gradient in VE–VCO₂ relationship are excluded from the analysis). In those cases in which there is not a sufficiently linear S₂ region, the first detectable point of VCO₂ acceleration relative to VO₂ can be used as an alternative AT estimator.

**Modified V-slope method** (Fig. 3). The modified V-slope method is an alternative to the V-slope method, which has particular utility when the VCO₂–VO₂ relationship cannot be partitioned into two linear segments (i.e. a curvilinear response), which is common. This is based on the assumption that the S₁ slope should have a value of 1.0 or less (the highest respiratory quotient, for carbohydrate, being 1.0) and that the S₂ slope should have a value >1.0 (because of excess VCO₂). Ensuring that the VO₂ and VCO₂ axes are scaled identically, the effective S₁–S₂ inflection point can be estimated by ‘running in’ a unitary tangent or ‘line of one’ (i.e. line with gradient ΔVCO₂/ΔVO₂ = 1.0) from the right until it first impacts on the VCO₂ – VO₂ relationship. The VO₂ at which this occurs is taken as the AT, as all higher data points manifest excess VCO₂ (i.e. with ΔVCO₂/ΔVO₂ > 1.0).

The V-Slope and modified V-slope methods depend solely on the physicochemical reaction of metabolically-produced hydrogen ions with bicarbonate and as such the occurrence of the breakpoint is independent of chemoreceptor sensitivity and the ventilatory response to exercise. The V-slope methods are therefore particularly useful for AT estimation in conditions characterized by poor respiratory chemosensitivity or premature respiratory–mechanical limitation that prevent
the development of a discernible \( \dot{V}E \) response to excess \( VCO_2 \) (e.g. chronic obstructive pulmonary disease). 84

**AT Criterion 2**: Hyperventilation relative to \( O_2 \): the ventilatory equivalent for \( O_2 \) and end tidal \( PO_2 \) at the AT (Fig. 4)

At the AT, the excess \( VCO_2 \) generated from anaerobic glycolysis results in a proportional increase in \( \dot{V}E \). There is no equivalent increase in \( \dot{V}O_2 \) at this point. Consequently \( \dot{V}E \) is driven by \( VCO_2 \) and starts to increase at a greater rate with respect to \( \dot{V}O_2 \); i.e. hyperventilation relative to \( O_2 \). This is
### Patient Details:

**Indication for Referral and specific clinical question:**

**Medical History:**

**Medications:**

**Baseline Observations:**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Ideal Weight</th>
<th>BMI</th>
<th>Hb</th>
</tr>
</thead>
</table>

### Exercise protocol and test conduct:

<table>
<thead>
<tr>
<th>Incremental test gradient</th>
<th>Watts/min</th>
<th>Incremental phase duration: minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test quality</td>
<td>good/poor and reasons</td>
<td></td>
</tr>
<tr>
<td>Perceived exertion (Borg scale, range: 1-10)</td>
<td>Borg, rest:</td>
<td>Borg, peak exercise:</td>
</tr>
<tr>
<td>Reason exercise stopped</td>
<td>Patient’s reason and Investigators’ observations</td>
<td></td>
</tr>
</tbody>
</table>

### Exercise Capacity: Anaerobic Threshold and \( \dot{V}O_2^{peak} \)

<table>
<thead>
<tr>
<th>( \dot{V}O_2^{peak} )</th>
<th>Absolute ml/min</th>
<th>ml/kg/min</th>
<th>% of predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaerobic threshold</td>
<td>Absolute ml/min</td>
<td>ml/kg/min</td>
<td>% of ( \dot{V}O_2^{peak} )</td>
</tr>
<tr>
<td>WR</td>
<td>At AT</td>
<td>Watts</td>
<td>At ( \dot{V}O_2^{peak} )</td>
</tr>
<tr>
<td>RER at peak exercise</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Cardiovascular Function:

<table>
<thead>
<tr>
<th>Resting ECG</th>
<th>Ischaemia or arrhythmia or conduction defect – when this occurred during test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise ECG</td>
<td>(normal approximately 220 – age bpm)</td>
</tr>
<tr>
<td>Predicted maximum HR</td>
<td>Absolute and % of maximum predicted value</td>
</tr>
<tr>
<td>BP</td>
<td>Rest: mm Hg</td>
</tr>
<tr>
<td>Peak HR</td>
<td>Absolute and % of predicted maximum heart rate</td>
</tr>
<tr>
<td>Heart rate reserve</td>
<td>Absolute and % of predicted peak exercise value; comment on profile of response</td>
</tr>
<tr>
<td>( O_2 ) pulse</td>
<td>Absolute and % of predicted peak exercise value; comment on profile of response</td>
</tr>
<tr>
<td>( \dot{V}O_2/NWR )</td>
<td>ml/min/watt (normal range 10 ml/min/watt; standard deviation +/- 1) comment on profile of response</td>
</tr>
</tbody>
</table>

### Respiratory Function:

<table>
<thead>
<tr>
<th>Breathing Reserve</th>
<th>Absolute and percentage (normal &gt; 15% or greater than 11 l/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( VE/VCO_2 ) at Anaerobic Threshold</td>
<td>(normal &lt; 32)</td>
</tr>
<tr>
<td>( VE/VCO_2 ) gradient</td>
<td>(normal &lt; 32)</td>
</tr>
<tr>
<td>Oxygen saturation</td>
<td>Rest %</td>
</tr>
<tr>
<td>Spirometry</td>
<td>FEV(_1), absolute and % predicted, FEV(_1)/FVC, MVV calculated (e.g. FEV(_1) x 40)</td>
</tr>
</tbody>
</table>

### SUMMARY: (containing the following information)

1. Exercise capacity – \( \dot{V}O_2^{peak} \) and Anaerobic Threshold and comment on normality or otherwise
2. Cause(s) of limitation of exercise capacity & abnormalities in the exercise response – eg cardiac limitation, respiratory limitation, mixed picture, deconditioning
3. Risk implications for the perioperative period – estimations of mortality and morbidity risk
4. Suggested pre-operative optimization/referrals eg optimise atrial fibrillation rate control and plan
5. Suggested location of perioperative care eg level 2 high dependency or ward.
reflected in $\dot{V}E/\dot{V}O_2$ and alveolar end-tidal $P_O_2$ ($P_{ETCO_2}$) both starting to increase at the AT. Thus at the AT the following occur: (1) the $\dot{V}E/\dot{V}O_2 - \dot{V}O_2$ relationship having been flat or decreasing to a nadir begins to increase systematically and (2) the $P_{ETCO_2} - \dot{V}O_2$ relationship having been declining or flat begins to increase systematically.

**AT Criterion 3**: no hyperventilation relative to CO2: the ventilatory equivalent for CO2 and end tidal co2 at the AT

The $\dot{V}CO_2 - \dot{V}O_2$ (V-slope) relationship and hyperventilation relative to oxygen do not alone provide a sufficiently rigorous criterion for AT estimation. It is important that non-specific hyperventilation (with an attendant fall in arterial $P_{aCO_2}$) due to factors such as anxiety, pain, or arterial hypoxaemia is first excluded as a cause of the excess $\dot{V}CO_2$ identified by the V-slope method. This requires examination of the ventilatory consequences of the excess $\dot{V}CO_2$. Below the AT, VE is proportional to $\dot{V}CO_2$ such that alveolar end-tidal $P_{CO_2}$ ($P_{ETCO_2}$) and arterial $P_{CO_2}$ remain stable. This proportionality is initially maintained above the AT because the normal compensatory hyperventilation expected with an exercise-induced metabolic acidosis (which lowers the $P_{aCO_2}$ and thereby compensates for the falling pH) does not occur immediately at the AT for rapid incremental exercise. Rather, respiratory compensation is delayed to a somewhat higher WR—defined as the RCP. The exact location of the RCP depends on factors such as the WR incrementation rate and peripheral (carotid body) chemoreflex responsiveness.

This delay, which is possibly consequent to slow carotid chemosensory response kinetics generates a phase of ‘isocapnic buffering’ between the AT and RCP within which neither $P_{ETCO_2}$ nor $P_{aCO_2}$ decline (i.e. there is no immediate hyperventilation relative to CO2 at the AT). To ensure that the inflection point identified as the AT is not as a result of non-specific hyperventilation that could be from pain, hypoxaemia or primary hyperventilation syndrome, hyperventilation relative to CO2 at the AT must be excluded by confirming the following: (1) $\dot{V}E/\dot{V}CO_2$ remains constant or continues to

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**Fig 6.** Example of a nine-panel CPET display for the normal individual depicted in Figures 2–4 (modified European Respiratory Society format). TOP ROW: panel 1: $\dot{V}CO_2$ vs $\dot{V}O_2$; Panel 2: $\dot{V}O_2$ vs work rate; and Panel 3: HR and $O_2$ pulse ($\dot{V}O_2$/HR error should read $\dot{V}O_2$/HR). SECOND ROW: Panel 4: $\dot{V}E/\dot{V}CO_2$ and $\dot{V}E/\dot{V}O_2$ vs $\dot{V}O_2$; Panel 5: $\dot{V}E$ vs $\dot{V}CO_2$; and Panel 6: $\dot{V}E$ vs $\dot{V}O_2$. BOTTOM ROW Panel 7: $P_{ETCO_2}$ vs $\dot{V}O_2$ (SpO_2 may be included); Panel 8: RER vs $\dot{V}O_2$; and Panel 9: unassigned, but here showing $\dot{V}E/\dot{V}O_2$ and $\dot{V}E/\dot{V}CO_2$ vs time. Suggested clusters for interpretation: AT estimation (green vertical line), [panels: 1,4,7 (and 9)] cardiovascular limitation, (panels: 2,3,5) respiratory limitation, (panels: 4,5,6 and 7). RER, Respiratory exchange ratio. See text for further details.
decrease at the AT as the $VE/VCO_2$ starts to rise systematically and (2) the absence of a fall in $P_{ET}CO_2$ at the AT. This is because ventilatory compensation for the metabolic acidosis above the AT which causes a reduction in $P_{ACO_2}$ does not occur until several minutes later during rapid incremental exercise tests (i.e., at RCP).

Above the RCP towards the end of the exercise test, the $VCO_2 - VO_2$ and $VE - VCO_2$ relationships steepen, as respiratory compensation develops in response to the metabolic acidosis of exercise; i.e., reflecting the loss of CO2 from arterial stores as $P_{ACO_2}$ is driven down by hyperventilation.

**Anaerobic Threshold Identification (Table 6 for summary)**

In summary, rigorous AT estimation requires that support be sought not only from excess $VCO_2$ but also from the profiles of the ventilatory equivalents and end-tidal partial pressures for O2 and CO2 to establish the development of hyperventilation relative to O2 but not with respect to CO2. This requires the demonstration that, coincident with the modified V-slope break point, $VE/VCO_2$ and $P_{ET}O_2$ start to increase (i.e., hyperventilation relative to O2), but with no coincident increase in $VE/VCO_2$ or decrease in $P_{ET}CO_2$ (i.e., no hyperventilation relative to CO2). In practice, it can be the case that noisiness in the data set may preclude reliable discrimination of all three break points simultaneously, in which case greater weight should be placed on the V-slope indices.

**Automated Anaerobic Threshold**

The V-slope method is used in the majority of commercial metabolic carts to identify an automated AT. These automated ATs should only ever be used as a guide and should be interpreted with caution. In the presence of a curvilinear $VCO_2 - VO_2$ relationship linear regression may not accurately identify the AT. In addition, care should be taken to ensure that the kinetic phase at the start of the incremental ramp and the portion of the data above the respiratory compensation point are excluded from the regression analysis, which requires manual interrogation of the data. Finally, automated V-slope methods do not use confirmation of the AT by the ventilatory criteria discussed above and thus, particularly in the presence of noisy data, may not accurately identify the AT.

**Anaerobic Threshold - False positives or pseudothresholds**

Transient volitional hyperventilation occurring just prior to the start of a ramp exercise test or in its early stages can compromise AT estimation and cause a pseudothreshold, where the criteria for an AT can be identified but before the onset of the exercise-induced metabolic acidosis. In such circumstances, acute hyperventilation causes acute wash-out of CO2 from rapidly exchanging body stores. Consequently, at the start of the test, a greater-than-normal proportion of the metabolic CO2 production will initially be diverted into the depleted body stores to recharge them back to normal levels, with less therefore reaching the lungs and less being cleared at the mouth. Over this period, the $VCO_2 - VO_2$ slope and RER are thus abnormally low. When the CO2 stores have subsequently been repleted, CO2 and RER will be restored towards normal levels, resulting in a relative steepening of the $VCO_2 - VO_2$ relationship and an apparent threshold. This relative acceleration of CO2 relative to VO2 will, in turn, elicit proportional increases in $VE$ and therefore $VE/VCO_2$, but no change in $VE/VCO_2$. This creates threshold-like behaviour (i.e., the standard non-invasive criteria for AT discrimination are met) but at a time when arterial (lactate) has not yet started to increase. The clue to pseudothreshold behaviour is a concurrent systematic fall in RER to abnormally low values (consequent to the transiently high CO2 storage rate) immediately prior to the supposed threshold. Thus, the presence of prolonged volitional hyperventilation immediately prior to or at the start of a ramp test requires the AT estimate to be interpreted with caution.

**Normal values and indexing exercise capacity variables**

Several series of reference values for incremental exercise test indices including $VO_2peak$ have been published. The most widely used in clinical practice are those produced by Hansen and Jones. These values were obtained from North American populations and have not been specifically validated in a UK surgical population. With these limitations in mind, reference values are useful to identify an abnormal response and the reference values used should be standardized within a CPET laboratory. A common convention used to relate measured $VO_2peak$ to reference values is: >>>80% not abnormal or within the 95% confidence interval; 71–80% mildly reduced; 51–70% moderately reduced; and < 50% severely reduced. It should be appreciated however that the majority of clinical cohorts in surgical patients have reported $VO_2peak$ as an absolute value indexed to body weight rather than as a percentage of predicted value. As a consequence the published risk thresholds for surgical patients preoperatively are absolute values of AT and $VO_2peak$ indexed to body weight. Indexing to body weight may have implications for patients at extremes of bodyweight, potentially over-estimating risk in the morbidly obese patient and under-estimating risk in cachectic patients. Despite this consideration, in morbidly obese bariatric patients, AT indexed to absolute body weight was more predictive of outcome than AT indexed to body surface area or to ideal body weight. Caution should be used when interpreting exercise capacity values indexed to body weight in patients with a low BMI. Indexing to ideal bodyweight may be considered.

**Ventilatory equivalents for carbon dioxide $VE/VCO_2$**

The ventilatory equivalent for carbon dioxide ($VE/VCO_2$) is the ratio of minute ventilation ($VE$) to CO2 output ($VCO_2$) and as such is an index of ‘ventilatory efficiency.’ Greater-than-normal values indicate that either the physiological dead space fraction of the breath (dead space/tidal volume, reflective of pulmonary gas exchange efficiency) is abnormally increased, $P_{ACO_2}$ is decreased (e.g., acute hyperventilation), or both. Thus, $VE/VCO_2$ gives insight into the efficiency of ventilation—perfusion matching in the lung and the efficiency of gas exchange. The slope of the linear $VE/VCO_2$ relationship $\Delta VE/\Delta VCO_2$, the ventilatory equivalent for CO2 at the AT ($VE/VCO_2AT$) or, if the AT cannot reliably be estimated, the minimum value of $VE/VCO_2$ ($VE/VCO_2min$) are numerically similar. This allows the investigator to choose which of the three is most amenable to measurement in the test. The values are elevated in heart failure, respiratory disease, and pulmonary hypertension. Furthermore, elevated $VE/VCO_2$ is predictive of mortality and disease progression in cardiac failure, and mortality and other outcomes in chronic obstructive pulmonary disease and other respiratory diseases. In the perioperative setting, $VE/VCO_2$ at the
anaerobic threshold is associated with morbidity and mortality in hepatobiliary surgery, abdominal aortic aneurysm surgery, urological surgery, and mixed surgical cohorts. Recent thoracic surgical cohorts suggest the $\dot{V}E/\dot{V}CO_2$ slope may be more predictive of postoperative mortality and pulmonary complications than $\dot{V}O_2\text{peak}$, although this requires further clarification. However, an association between $\dot{V}E/\dot{V}CO_2$ and surgical outcome has not been identified in all cohorts, with some studies reporting no predictive association. Further studies are required to clarify the additional risk conferred by abnormal ventilatory efficiency in addition to impaired exercise capacity.

The perioperative CPET report (Grade C, good practice recommendations, unless otherwise stated)

It is recommended that the perioperative CPET report includes: (1) reason for referral, relevant past medical history, and drug history; (2) CPET data, presented in tabular form and graphically; (3) a description of the patient’s exercise capacity and its normality or otherwise; (4) a summary of the cause(s) of exercise limitation if exercise capacity is abnormal; (5) a statement about the risk implications of the exercise limitation and other identified abnormalities (Grade D); and (6) suggestions for possible referrals and interventions preoperatively (Grade D).

An example of a tabular report with a suggested minimum data set is presented in Fig. 5. In addition it is conventional practice to present CPET data graphically in the report in a multipanel format, typically with eight or nine panels (Fig. 6). It should be emphasized that the difference between the original Wasserman and the European Respiratory Society formats lies more in data presentation rather than in overall content. An advantage of the European Respiratory Society format in the perioperative setting is that the panels required for AT estimation are conveniently placed in a single column to aid discrimination decisions across the three criterion indices (a practice that has been adopted in the updated Wasserman 2011 format13). For this reason, the European Respiratory Society format tends to be preferred for perioperative CPET, with the option for including a ninth panel as a non-assigned panel that can usefully be used for tailoring test results to allow, for example, tracking of temporal responses of interest (Fig. 6). Interpretation with regard to normality is done against published normal-value databases and algorithms.1,4,15

Risk thresholds in perioperative CPET

Specific recommendations about risk thresholds and recommendations for perioperative care are outside the remit of these guidelines. As surgical and perioperative practice evolves, risk thresholds are likely to change. Furthermore, it is likely that the variables used to predict risk are likely to evolve and expand. Practitioners should evaluate local data and published cohorts on a regular basis to guide these recommendations. Further research is required to accurately enumerate the absolute risk of morbidity and mortality associated with different levels of functional capacity. National data collection is planned by POETTS, to provide access to contemporaneous risk threshold data. A summary of current case cohorts is presented in Supplementary Appendix S2.

Summary

The dynamic metabolic challenge imposed by perioperative CPET provides an objective means of evaluating exercise capacity. It can be used to evaluate chronic comorbidities and may enable identification of new pathology that requires treatment, optimization, or both preoperatively. The data derived from CPET may be used to inform collaborative (shared) decision-making and the process of consent, to triage patients to high dependency care, and to direct individualized exercise training programmes pre- and postoperatively. If CPET data are to help determine surgical patients perioperative care, it is essential that CPET procedures are reproducible and of high quality. This requires laboratory equipment to be maintained, calibrated, and validated regularly. Standardized exercise protocols with standardized graphical display of key variables to describe exercise capacity, and to investigate possible causes of exercise intolerance should be employed. These guidelines provide direction for clinicians performing and interpreting CPET on perioperative patients.

Authors’ contributions


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Declarations of interest


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Appendices: Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.bja.2017.10.020.
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