

How to Interpret a CRF Assessment – Key Measures that Provide the Best Picture of Health, Disease Status and Prognosis

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Abbreviations

ACC – American College of Cardiology

AHA – American Heart Association

CO – Cardiac output

CPET – Cardiopulmonary exercise testing

CRF – Cardiorespiratory fitness

CVD – Cardiovascular disease

iCPET – Invasive cardiopulmonary exercise testing

ECG – Electrocardiogram

EOV – Exercise oscillatory ventilation

FRIEND – Fitness Registry and the Importance of Exercise

HF – Heart failure

MET – Metabolic equivalent of task

RPE – Rating of perceived exertion

VD/VT – Dead space to tidal volume ratio

VE/VCO₂ – Ventilation to carbon dioxide ratio

VHD – Valvular heart disease

VO₂ – Oxygen consumption

Abstract

Graded exercise testing is a widely accepted tool for revealing cardiac ischemia and/or arrhythmias in clinical settings. Cardiopulmonary exercise testing (CPET) measures expired gases during a graded exercise test making it a versatile tool that helps reveal underlying physiologic abnormalities that are in many cases only present with exertion. It also characterizes one's health status and clinical trajectory, informs the therapeutic plan, evaluates the efficacy of therapy, and provides submaximal and maximal information that can be used to tailor an exercise intervention. Practitioners can also modify the mode and protocol to allow individuals of all ages, fitness levels, and most disease states to perform a CPET. When used to its full potential, CPET can be a key tool used optimize care of in primary and secondary prevention settings.

Keywords: Exercise testing, Cardiorespiratory fitness, Cardiopulmonary

Introduction

Cardiopulmonary exercise testing (CPET) has been a longstanding tool that holds high diagnostic and prognostic utility. A standard exercise test is commonly used to reveal ischemia or exertional dysrhythmias in clinical settings, but the addition of expired gas analysis can expand the diagnostic capabilities that help determine the origin of one's symptoms and/or complaints by interpreting data acquired at rest, exercise, and recovery. Thus, it helps expand a practitioner's understanding of a patient's health status beyond what is known from resting vital signs by quantifying the cardiopulmonary and peripheral systems' ability to synergistically function to reach the body's peak levels. Although seemingly simple, there are many considerations related to selecting the correct mode and protocol for the individual being tested, understanding equipment capabilities, as well as interpreting singular and comprehensive markers of interest. Practitioners must therefore have a deep understanding of these topics to proficiently apply CPET in the clinic.

Accordingly, we will review the equipment and data that can be collected during a CPET, how measures can be used in athletic individuals, those with cardiovascular disease (CVD), pulmonary disease, or end stage organ disease.

CPET Equipment and Data

The assessment of cardiorespiratory fitness (CRF) in applied settings can be accomplished through the minimal use of equipment with little to no associated costs but at the risk of greater variability/inaccuracy, or with medical grade equipment at a higher cost with the added benefit of accuracy, precision, and broad evaluation of clinically relevant variables. For the purposes of this paper, we will briefly review standard CPET equipment and measures that are commonly acquired through their use. To observe and characterize hemodynamic, oxygen

saturation, cardiac rhythm and electrical activity responses to exercise, a manual blood pressure cuff, pulse oximeter, and 12-lead electrocardiogram (ECG) monitor are needed, respectively. A metabolic cart is required to objectively quantify the cardiorespiratory responses to exercise. Although CPET provides accurate and reproducible noninvasive data across metabolic carts, subtle differences in equipment technical/functional capabilities should be understood to ensure quality of data collected and reported. Factors related to equipment standards (i.e., maintenance, calibration) that may affect data acquisition have previously been thoroughly described.¹ Lastly, an aerobic exercise modality, such as a treadmill, cycle ergometer, or an arm ergometer in some settings that frequently evaluate non-ambulatory individuals is needed to appropriately exert individuals to volitional fatigue.

CPET is most often performed using a treadmill or cycle ergometer in clinical settings, each presenting unique attributes that alter exercise response. Of note, CPET performed on a treadmill typically elicits a greater cardiovascular and metabolic response with higher maximal oxygen uptake (VO_2), heart rate, systolic blood pressure, rate pressure product, and cardiac output (CO) compared to cycle ergometry^{2, 3}. However, CPET performed on a cycle ergometer should be pursued for those with balance instabilities or orthopedic, ambulatory, and peripheral vascular concerns in order to exert their cardiopulmonary system safely and adequately. Due to reduced muscle mass utilization and localized leg fatigue, cycle ergometers elicit approximately 9% lower maximal metabolic equivalent of task (MET) compared to the treadmill⁴. Despite this, less auditory artifact during manual blood pressure assessment, reduced ECG artifact, and capture of work rate measures may make the cycle ergometer an appealing testing modality for many testing facilities^{2, 3}. Careful consideration of patient characteristics, research/clinical objectives, and safety concerns is needed before selecting the appropriate testing modality.

Metabolic carts utilize one of two primary methods for gas analysis: breath-by-breath and mixing chamber, each with distinct advantages and limitations in capturing ventilatory data. Breath-by-breath enables the capture and assessment of breathing patterns and fluctuations in ventilatory gas exchange in real-time. It also enables identifying rapid changes and breath-by-breath variability. However, breath-by-breath measurement is susceptible to errors from breathing patterns and equipment calibration. Mixing chamber measurement allows for collecting and analyzing breath samples in a closed chamber over a short period of time. Despite providing more accurate average gas concentrations, mixing chamber systems cannot capture dynamic changes that occur with breathing. Table 1 provides a breakdown of breath-by-breath and mixing chamber ventilatory capabilities.

During a CPET, hemodynamic responses can be measured directly through heart rate, blood pressure, rate pressure product, and oxygen pulse. Indirect inferences of stroke volume can be made by dividing VO_2 with the corresponding heart rate across CPET stages. It's also helpful to monitor subjective experiences, such as rating of perceived exertion (RPE), chest pain, dyspnea, and fatigue, using standardized scales to assess physiological symptoms during the CPET.⁵

A higher level of systemic evaluation can be pursued through the use of CPET with Doppler echocardiography or invasive CPET (iCPET). CPET with Doppler echocardiography allows for a detailed assessment of cardiac contractility and relaxation as well as an assessment of valvular function. However, these additional assessments are time intensive, require specialized staff and equipment, and are indicated for a smaller proportion of patients. Briefly, iCPET involves the insertion of pulmonary and radial artery catheters allowing direct measurement of cardiac filling pressures, pulmonary artery pressures, and cardiac output.

Additionally, a separate catheter can be placed peripherally at the wrist to directly assess blood oxygen and carbon dioxide levels, pH, and lactic acid to evaluate peripheral tissue oxygen extraction. Collectively, these measures enhance the ability to identify difficult to diagnose conditions such as exercise-induced pulmonary arterial hypertension, exercise-induced heart failure (HF) with a preserved ejection fraction, and preload failure. Detailed information regarding these assessments is documented elsewhere.⁶⁻⁹

Predicting Performance and Putting Results into Perspective

In many clinical settings, it has been commonplace to follow a one size fits all approach to selecting exercise testing protocols. Often times, this method leads to selecting protocols that are too aggressive for the relatively low fit patient being tested, resulting in an inadequate examination of their response to exercise. Instead, the recommended approach is to select a protocol where the patient reaches volitional fatigue in 8 to 12 minutes. This process can be facilitated by using population specific prediction equations to determine a likely peak VO_2 based on readily available patient characteristics found within their medical records or a health history questionnaire/interview.¹⁰⁻¹²

Cardiopulmonary and hemodynamic responses at peak exercise occur over a wide range of values and are impacted by age, sex, exercise modality, physical activity level, sedentary behavior, and health status to name a few. Interpreting common measures acquired during CPET may seem arbitrary to the untrained practitioner and patient. Comparing various clinical outcomes to reference values based on data collected in a large and ideally heterogenous group is an initial step to bringing clarity to CPET interpretation. Currently, the Fitness Registry and the Importance of Exercise (FRIEND) national database is widely utilized for these purposes. This registry boasts over 22,000 unique tests accumulated from nearly 40 testing laboratories across

the nation and has reference values for peak VO_2 , blood pressure, ventilation, ventilation to carbon dioxide ratio (VE/VCO_2), oxygen pulse, and rating of perceived exertion.¹³⁻²²

Clinical Applications of CPET

Sports cardiology

Sports cardiology is a diverse, evolving sub-specialty of cardiology that is gaining more attention and popularity. It encompasses the care of physically active individuals that have or may be at risk for CVD, understanding the physiologic adaptations and potential pathology that comes with exercise and sports, and involves optimizing physical fitness for desired performance goals. CPET can serve an important role in diagnostic evaluation as well as for providing exercise and training guidance. Although, a standard CPET may often adequately stress various physiologic systems to reveal pathophysiology, a non-traditional approach may be needed to reproduce symptoms by mimicking training mode, conditions, intensities, and duration in this high functioning population.²³

Athletic patients can present with a variety of exertional complaints from chest pain, shortness of breath, palpitations, and lightheadedness to unexplained decline in athletic performance. In younger patients, congenital anomalies including hypertrophic cardiomyopathy, long-QT syndrome, and coronary artery anomalies can provide risk while exercising. In older individuals, CVD such as coronary artery disease, valvular disease, HF with reduced or preserved ejection fraction, pulmonary vascular disease, and cardiomyopathies is prevalent and has been the leading cause of death in the United States.²⁴ Although regular exercise is protective against the development of many cardiovascular disorders, it does not confer complete immunity, and athletic patients should be evaluated with a commensurate level of concern as the

general population. Moreover, given that certain exercise can cause harm in many cardiac disorders, it is crucial to comprehensively rule out or diagnose cardiac conditions.

Along with the resting ECG and echocardiogram, CPET is an invaluable prognostic tool used by sports cardiologists. With an integrated hemodynamic assessment of the cardiac, pulmonary, vascular, and muscular systems, CPET can help direct the clinical evaluation with often ambiguous symptoms such as shortness of breath or performance decline. Another benefit of CPET, compared to other popular diagnostic exertional testing modalities such as a stress echocardiography, is that CPET allows for clear graphical evaluation through peak exercise. Many patients, especially those who are trained athletes, will have a rapid reduction in their heart rate after exercise which limits the ability to capture appropriate peak exercise images in modalities such as stress echocardiography.

Whether CPET is being performed for diagnostic, transplant clearance, return to play clearance, or as a part of one's annual checkup, the extensive hemodynamic and cardiopulmonary data can also be leveraged when prescribing volumes of activity aimed at improving CRF.^{25,26} In patients with significantly elevated, life-long risk with exercise such as those with arrhythmogenic right ventricular dysplasia, catecholaminergic polymorphic ventricular tachycardia, or high-risk hypertrophic cardiomyopathy, defining anaerobic threshold (also known as lactate or ventilatory threshold) can be very important.²⁷⁻²⁹ Using CPET to determine anaerobic threshold can define a threshold between "moderate" and "high" intensity exercise, with the latter conferring increased arrhythmogenic stressors. Individuals with such disorders are often recommended to keep their exercise intensity at a moderate range or lower.

Cardiac impairment and prognosis

Graded exercise testing has been extensively employed in populations with or suspected CVD. The addition of expired gas analysis has contributed to a more robust clinical evaluation of this population that has helped guide therapeutic decision making. Among the various measures, VE/VCO₂ slope is the most frequently studied index of ventilatory efficiency but can also be reported at the anaerobic threshold or at its nadir.³⁰ Mechanisms for elevated VE/VCO₂ are multifactorial and include ventilation-perfusion mismatch, reduced cardiac output, high dead space to tidal volume ratio (VD/VT), arterial hypoxemia and metabolic acidemia.³¹ Elevated VE/VCO₂ is prognostic in a number of cardiac conditions described below.

The utility of CPET to determine prognosis in HF was established decades ago by multiple studies such as work by Mancini et al. examining the value of peak VO₂ for estimation of risk in patients with advanced HF due to systolic dysfunction.^{32, 33} In cardiac transplantation candidates, a peak VO₂ greater than 14 ml/kg/min suggested transplant could be safely deferred due to similar 1- and 2-year survival rates as those who received transplant.³² Peak VO₂ ≤14 ml/kg/min remains a transplant listing criteria for those not on beta blocker therapy; ≤12 ml/kg/min is the cut point for those on beta blockers and with devices (if the test is submaximal (respiratory exchange ratio <1.05), VE/VCO₂ slope >35 may be a criterion for listing).³⁴ Additionally, peak VO₂ and VE/VCO₂ slope are strong independent predictors of prognosis and were identified as significant predictors of mortality and hospitalization in patients with systolic HF and diastolic HF, however, after multivariate analysis VE/VCO₂ was the only predictor in diastolic HF (regardless of left ventricular ejection fraction).^{35, 36} Moreover, peak VO₂ <10 ml/kg/min and VE/VCO₂ slope ≥45 portends poor prognosis in the two years after testing.³⁷ Finally, exercise oscillatory ventilation (EOV) is prevalent in patients with HF and is a strong

predictor of mortality and when combined with elevated VE/VCO₂ slope the risk increases significantly (Hazard ratio 11.4).³⁸⁻⁴⁰

In patients with valvular heart disease elevated VE/VCO₂ slope is useful for determining the presence of elevated pulmonary pressures which are a consequence of left-sided valvular disease.⁴¹ Additionally, elevated VE/VCO₂ slope in asymptomatic severe aortic stenosis is a significant predictor of mortality and decompensated HF.⁴² Furthermore, in patients with asymptomatic aortic stenosis development of symptoms or a decrease in blood pressure during exercise represent indications for aortic valve replacement (European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines).⁴³ CPET is recommended as part of standard evaluation in patients with hypertrophic cardiomyopathy to elucidate severity and mechanism of functional limitation (Class of Recommendation 1-2b, according to symptom level).⁴⁴ In patients with hypertrophic cardiomyopathy, low peak VO₂ (<80% of predicted), ventilatory anaerobic threshold and elevated VE/VCO₂ slope (>34) are prognostic for increased risk of major events (septal reduction therapy, progression to advanced HF, death from HF, and heart transplant, and all-cause mortality).^{44, 45} However, for each 1 ml/kg/min increase in peak VO₂ and ventilatory anaerobic threshold, the risk of death or transplant was reduced by 21% and 29%, respectively.⁴⁵ Conversely, each 1 unit increase in VE/VCO₂ is associated with 18% increased risk of death or transplant.⁴⁵

The use and value of CPET has grown in recent decades for evaluation of adults with congenital heart disease. Responses to CPET are variable and due to the heterogeneity of congenital heart disease, however, a common finding is reduced exercise capacity compared to healthy adults.^{46, 47} Peak VO₂ is prognostic for risk of hospitalization and mortality.⁴⁷ VE/VCO₂

slope can represent both cardiac and pulmonary impairment to exercise and in noncyanotic congenital heart disease patients (stratified into VE/VCO₂ slope quartiles) VE/VCO₂ slope ≥ 38 was a strong predictor of mortality (13% mortality at 2 years compared to only 1% in the other quartiles).⁴⁸

CPET has been utilized for perioperative and post-operative risk-stratification in those undergoing major intra-abdominal surgery, including cancer-related surgeries, and thoracic surgery.^{49, 50} Ventilatory threshold and VO₂ peak predict perioperative and post-operative complications. Specifically, ventilatory threshold predicts postoperative complications across numerous surgical specialties more accurately than other CPET variables.⁴⁹ Elevated VE/VCO₂ was associated with morbidity and mortality in some case series but others reported no association.⁵¹ In patients with lung cancer undergoing resection, those with a VO₂ greater than 20 ml/kg/min were at low risk of surgical complications and mortality and those with a VO₂ less than 10 ml/kg/min were at high risk of morbidity and mortality postoperatively.⁵²⁻⁵⁶

Delay in recovery of post-exercise VO₂ or plateau/increase of VO₂ into recovery reflects abnormal oxygen kinetics and cardiac impairment to exercise.⁵⁷⁻⁶⁰ This delay represents the repayment of the oxygen deficit created because of cardiac output limitation that failed to compensate for the metabolic demands of exercise.⁶¹ Plateau of VO₂ into recovery is an independent predictor of cardiac transplant-free survival in patients with HF, and for every ten second increase in the delay, the hazard ratio for cardiac transplantation and death increased by 37%.⁶¹

Oxygen pulse is a surrogate for left ventricular stroke volume and represents oxygen consumed per heartbeat (VO₂/heart rate).^{62, 63} Normal oxygen pulse response to exercise is a quick increase in early exercise and continued, primarily linear increase throughout testing until

peak exercise.³⁰ A plateau or decline of oxygen pulse during exercise represents limited stroke volume augmentation and reflects cardiac impairment to exercise (may also reflect peripheral vascular perfusion/extraction limitation).^{30, 33} In the evaluation of myocardial ischemia, CPET improved diagnostic accuracy and plateau or flattening of oxygen pulse and VO_2 versus power slope were markers of myocardial ischemia.^{64, 65} This has been demonstrated in patients with myocardial ischemia but is prevalent in other conditions as an indicator of cardiac impairment to exercise.⁶⁴ Interpretation of oxygen pulse can be impacted by anemia and known abnormalities in O_2 extraction. The prognostic value of peak oxygen pulse has been demonstrated in a cohort of men without CVD, and not on beta blocker therapy, such that the peak oxygen pulse was inversely related to risk of death.⁶³

Pulmonary impairment and prognosis

Patients with pulmonary impairment often have similar presentations to patients with CVD, including reduced CRF and health related quality of life. Although pulmonary impairment is characterized by chronic airflow limitation, cough, and dyspnea, patients present with a large range of symptom severity, from unexplained or allergic mild dyspnea to severe complex symptoms seen in end stage lung disease. It follows that the spectrum of prognostic tools ranges from spirometry and timed walking tests to advanced imaging⁶⁶⁻⁶⁹.

In many cases, a diagnosis can be arrived at based on presentation, history and basic tests such as spirometry, blood screening, blood gas assessment and imaging (chest X-ray, computerized tomography and magnetic resonance imaging)⁷⁰. However, a presentation of shortness of breath or dyspnea on exertion can sometimes be difficult to diagnose, and prognosis in pulmonary disease can be especially challenging.

The application of CPET for patients with suspected and known pulmonary limitations has a long history, with seminal work in the field going back to the 1950s, including the introduction of the Wasserman 9 panel plots in the late 1980s⁷¹⁻⁷³. However, the use of data from CPET in pulmonary impairment continues to evolve and there is still much to be learned, and CPET remains poorly understood and underused in this population⁶⁶. CPET parameters such as peak VO_2 , VE/VCO_2 slope, and the first ventilatory threshold have been shown to correlate with disease severity, functional status, and mortality in pulmonary disease⁷⁴. Metrics like breathing reserve, VE/VCO_2 , end-tidal oxygen and end-tidal carbon dioxide and respiratory exchange ratio can help distinguish pulmonary disease from cardiac and other causes of shortness of breath/dyspnea on exertion. Other prognostic indications, such as the presence of oscillatory breathing and high VE/VCO_2 slope, which carry very poor prognosis in others may be more common in pulmonary dysfunction. If pulmonary disease is suspected, an ordered presentation of CPET results including, 1) perceptual response, 2) ventilatory control, 3) dynamic respiratory mechanics and 4) cardio-circulatory response has been suggested.^{75, 76} In addition, CPET provides valuable information on the mechanisms of exercise limitation in pulmonary dysfunction, such as ventilatory limitation and gas exchange impairment, as well as comorbid conditions such as cardiovascular dysfunction, morbid obesity and sedentary/detrained, among others.⁷⁷

CPET can also be used to assess the effectiveness of interventions aimed at improving exercise capacity in chronic obstructive pulmonary disease, such as pulmonary rehabilitation, pharmacological therapy, and oxygen supplementation^{78, 79}. Several studies have demonstrated that CPET parameters improve following these interventions, suggesting improved exercise capacity and cardiopulmonary function. For example, the effect of bronchodilation for patients

with chronic obstructive pulmonary disease has been shown to reduce dynamic hyperinflation as measured by improvements in inspiratory capacity during CPET, leading to improvements in cycle exercise endurance time of 20%.⁸⁰ Especially improvements in peak VO_2 and ventilatory efficiency, time to exercise intolerance and perceived exertion are thought to have the greatest impact on quality of life and ability to perform activities of daily living for patients with pulmonary limitations.⁸¹

To summarize, for the majority of individuals with suspected or diagnosed pulmonary disease, CPET is an appropriate and valuable prognostic tool, which can illustrate major physiological limitations, including restrictive/ obstructive pulmonary, central hemodynamic and peripheral. Importantly, the coexistence of cardiac and pulmonary impairment is common, especially among the least fit patients. Some more typical findings in patients with pulmonary disease (e.g. ventilatory inefficiency, exercise oscillatory breathing) likely indicate higher disease severity when in combination with cardiac disease. In all cases, CPET can guide treatment strategies, including exercise prescription, advanced imaging and transplant.

Transplant clearance (i.e., heart, kidney, lung)

The care of patients with advanced organ failure requires careful, accurate, and timely assessment of prognosis when being considered for transplant. Regarding patients with advanced HF, the 2022 American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America HF Guidelines and 2016 International Society for Heart Lung Transplantation listing criteria give a class I recommendation for CPET to determine the appropriateness of heart transplant.^{82, 83} While many variables derived from CPET have shown robust prognostic value among patients with HF, including VE/VCO_2 slope, EO_V, exercise uptake efficiency slope, and peak VO_2 . This recognition largely stems from the landmark study

from *Mancini et. al* as described earlier.^{32, 82} Moreover, peak VO_2 retains its prognostic value among patients on a beta blocker, though a more appropriate cut point of peak $\text{VO}_2 \leq 12$ ml/kg/min is used when considering transplant candidacy for these patients.⁸⁴

In addition to HF, measures of CRF have also demonstrated prognostic benefit among patients with advanced lung disease being considered for lung transplant. Recently, a new scoring system, named the lung composite allocation score, was implemented to match donor lungs to potential transplant candidates, with the goal of achieving more equitable lung allocation.⁸⁵ This new system accounts for medical urgency, likelihood of recipient survival at 5 years post-transplant, potential biological challenges in matching, candidate age, whether the candidate was a prior living organ donor, and placement efficiency. The lung composite allocation score includes the 6-minute walk test (6MWT) among the variables used to calculate the score. Additionally, different 6MWT criteria exist to help assess the timing of listing for lung transplant, depending on the specific lung disease. For example, desaturation to $<88\%$ on 6MWT or >50 meter decline in 6MWT over the past 6 months is used for interstitial lung disease, while 6MWT <400 meters is used for cystic fibrosis.⁸⁶

Among patients with end-stage renal disease being considered for kidney transplant, higher exercise capacity is associated with a reduced risk of cardiovascular events, conferring excellent prognosis among transplant candidates. CRF assessment occurs primarily when considering the patient's perioperative cardiovascular risk. Current AHA/ACC guidelines do not recommend any cardiac testing if the patient can achieve ≥ 4 MET of activity prior to undergoing transplant, regardless of their baseline level of cardiovascular risk.⁸⁷ If the patient cannot achieve at least 4 MET of activity, then a IIa recommendation is given for pharmacological stress testing.⁸⁷ However, many transplant centers do not adhere to these guidelines, despite emerging

evidence that revascularization for stable coronary artery disease in patients with chronic kidney disease does not reduce cardiovascular outcomes regardless of kidney transplant waitlist status.⁸⁸

Conclusion

CPET is a versatile tool that helps reveal underlying physiologic abnormalities only present with exertion, characterizes one's health status and clinical trajectory, informs the therapeutic plan, evaluates the efficacy of therapy, and provides submaximal and maximal information that can be used to tailor an exercise intervention. Practitioners can also modify the mode and protocol to allow individuals of all ages, fitness levels, and most disease states to perform a CPET. If used as intended, the CPET can be a vital aid in the management of patients before or after the development of chronic health diseases.

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Table 1. Variables acquired during a cardiopulmonary exercise test and respective data analysis between metabolic analyzers.

Ventilatory Variables	Breath-By-Breath	Mixing Chamber
Oxygen Consumption (VO_2)	Continuous, real-time, captures breath-by-breath variation	Averaged values over specific time intervals
Pulmonary Ventilation (VE)	Continuous, real-time, captures breath-by-breath variation, detects rapid changes in VE	Averaged values over specific time intervals, may not capture rapid changes in VE
Respiratory Exchange Ratio	Continuous, real-time, detects rapid changes in fuel utilization	Averaged values over specific time intervals, may mask transient fluctuations
Carbon Dioxide Production (VCO_2)	Continuous, real time, detects transient changes in CO_2 production	Averaged values over specific time intervals, may not capture breath-by-breath variability in CO_2
Ventilatory Equivalents for O_2 and CO_2 ($\text{VE}/\text{VO}_2, \text{VE}/\text{VCO}_2$)	Continuous, real-time, detects rapid changes in ventilatory response to metabolic demands	Averaged values over specific time intervals, may obscure the relationship between

		ventilation and metabolic variables.
End-tidal CO ₂ and O ₂ (P _{ET} CO ₂ , P _{ET} O ₂)	Real-time, captures breath-by-breath fluctuations in oxygen and carbon dioxide production	Averaged values over specific time intervals, may smooth out rapid fluctuations
Oxygen Pulse (O ₂ pulse)	Higher temporal resolution, detects rapid changes in VO ₂	Averaged values may smooth out rapid fluctuations.
Exercise Oscillatory Ventilation (EOV)	Continuous, real time, detects rapid fluctuations in ventilation	Averaged values over specific intervals, may smooth out rapid fluctuations
Ventilatory Threshold	Precise identification of ventilatory threshold	Averaged threshold values with may not pinpoint the exact moment threshold occurs
Ventilation-Perfusion (V/Q) ratio	Continuous analysis, detects rapid changes	Averaged ratio over specific time intervals, may not represent short-term variations