CPET-Insight

Clinician's Guide to Cardiopulmonary Exercise Testing

Measured & Derived Parameters

Cardiopulmonary exercise testing (CPET) is a comprehensive breath-by-breath assessment of heart, lung, and skeletal muscle function in real-time during exercise. It is the gold standard for quantifying cardiorespiratory fitness (CRF=Peak-VO2)) and determining the mechanism of exercise limitation

Metabolic Parameters

1. Workload

Work rate at peak exercise quantified in Watts. It represents the external work performed by the subject during a ramp incremental cycle ergometer test. Treadmills cannot quantify workload in terms of watts and is one reason they are not used when higher precision is needed.

2. VO_2 and VCO_2

Volume of oxygen consumed (VO_2) and carbon dioxide produced (VCO_2), measured at the mouth, expressed as liters/min or weight corrected as ml/kg/min. Under steady-state conditions, external respiration (VO_2 & VCO_2) equals cellular respiration in mitochondria of working skeletal muscles (QO_2 & QCO_2).

3. Metabolic Equivalents (METs)

Units used to quantify estimated work capacity when VO_2 is not directly measured. One MET equals 3.5 ml/kg/min of O_2 metabolized.

4. Respiratory Exchange Ratio (RER)

The ratio of VCO_2/VO_2 at any given point. RER is approximately 0.8 at rest, rises to ~0.95 at the anaerobic threshold, and reaches 1.10 or higher at peak exercise. A peak RER ≥ 1.10 signifies significant lactic acidosis and is the primary criterion for determining maximal effort — more accurate than peak heart rate alone.

Figure 1 — Cardiovascular Response to Exercise (Respiratory Exchange Ratio)

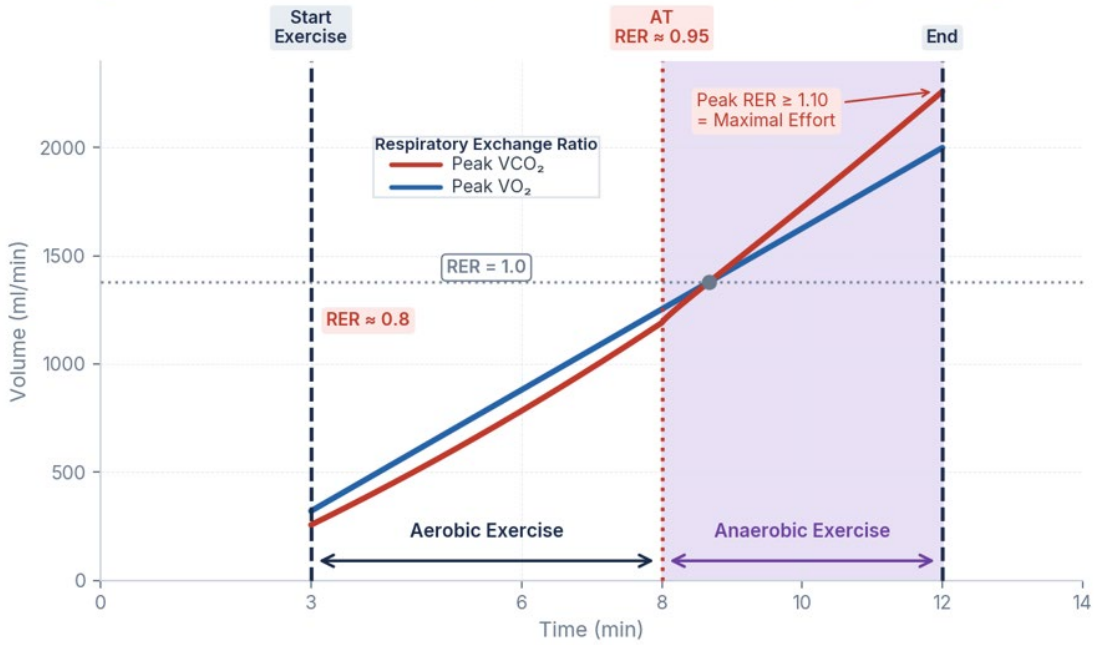


Figure 1 — Respiratory Exchange Ratio (RER) trajectory from rest to peak exercise. RER crosses 1.0 at the anaerobic threshold; ≥ 1.10 at peak confirms maximal effort.

5. Maximal Oxygen Uptake (VO_2-max)

VO_2-max is defined as a plateau in oxygen uptake (VO_2) despite an incrementally increasing workload at peak exercise. It represents the maximum aerobic work capacity of the muscles to metabolize oxygen. This can only be achieved when there is no cardiovascular or pulmonary limitation. Most apparently healthy individuals will not achieve their true VO_2-max due to cardiovascular limitation (O_2 supply limitation).

6. Peak Oxygen Uptake (Peak VO_2)

The highest VO_2 attained at peak exercise when no plateau is observed. It is the gold standard for quantifying exercise/functional capacity or cardiorespiratory fitness (CRF) and is the product of peak cardiac output and peripheral extraction (Fick's equation).

Peak VO_2 is the most robust predictor of all-cause mortality across all patient populations. In patients with cardiovascular, pulmonary, or skeletal muscle disorders, it quantifies disease severity as a direct linear function. Serial Peak VO_2 measurements serve as an effective surrogate marker for disease progression, regression, and response to therapy with patients acting as their own controls.

Predicted peak values are calculated using the Wasserman equation and are based on age, height, weight, and sex. Peak VO_2 can be expressed as L/min, mL/min, or mL/kg/min, and as Percent Predicted (%). The higher the percent predicted above 100%, the healthier the individual.

7. Anaerobic Threshold (AT)

The AT is the highest oxygen uptake achieved without a sustained increase in blood lactate. It is reached when cardiac output cannot supply adequate O_2 to the working skeletal muscles, thereby initiating anaerobic metabolism. The resulting lactic acidosis stimulates carotid body pH receptors, increasing minute ventilation to expel excess CO_2 to maintain blood pH homeostasis. It is expressed as the ventilatory anaerobic threshold (VAT) — the O_2 consumption (ml/kg/min) at the point CO_2 production increases.

The normal range for becoming anaerobic is between 40–60% of predicted peak VO_2. Values below 40% indicate inefficient O_2 delivery due to cardiac impairment or mitochondrial dysfunction (majority are due to cardiac impairment). AT is an effort-independent measure of functional capacity or CRF.

8. Inducible Threshold (IT)

If present, the IT will generally occur within 90 seconds of the AT. It marks a marked change in cardiac work efficiency to deliver O_2 to the peripheral tissues. Before the IT, cardiac output is driven primarily by stroke volume (SV) with less dependance on heart rate (HR) — a more energy efficient mechanism seen in athletes and healthy individuals.

IT marks the onset of mechanical dysfunction from myocardial energy (ATP) depletion, which results in an incremental decrease in stroke volume (decrease in slope, complete plateau, or decreasing trend). To compensate, the autonomic nervous system simultaneously up-regulates the HR response to maintain cardiac output and peripheral perfusion. This increased dependance on HR raises energy consumption per cardiac cycle, representing a sudden decrease in cardiac work efficiency.

Over time, persistent IT results in progressive decrease in Peak VO_2, quality of life, and longevity. The presence of an IT results in a decreased peak SV (peak O_2-pulse) and peak cardiac function (Peak VO_2). Reversing the IT results in increased cardiac work efficiency and higher peak values.

Clinical Significance: Reversing the IT can be documented on an individual basis and results in higher Peak O_2-pulse or Peak VO_2 or both, signifying improved cardiac function and long-term prognosis.

9. $\Delta VO_2/\Delta$Work Rate

The rate of oxygen uptake as a function of increasing linear workload. The slope should be linear and constant in normal individuals (~10.0 ml/min/watt). A value < 8.5 ml/min/watt signifies that cardiac output is not commensurate with peripheral oxygen demand — an important diagnostic parameter in moderate-to-severe heart failure.

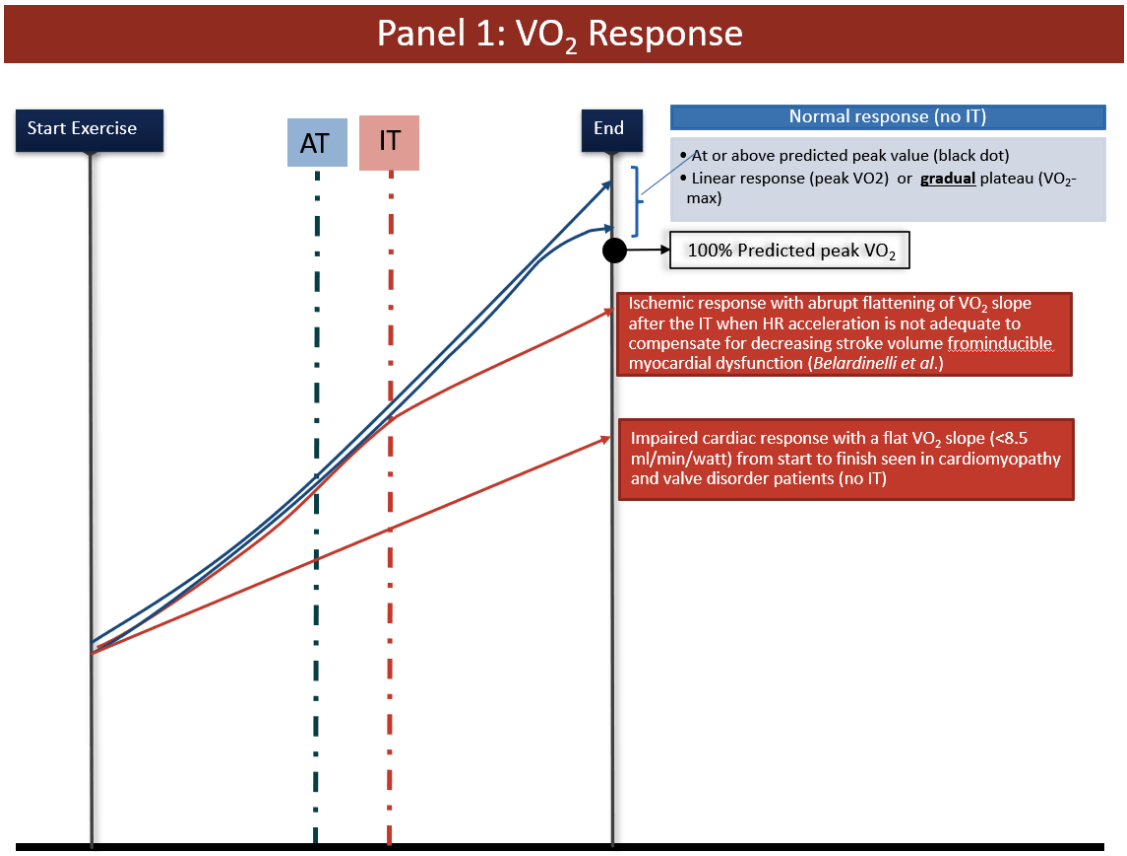


Figure 2 — $\Delta VO_2/\Delta WR$ slope. A normal slope of ~10 ml/min/watt (top line) versus an abnormal slope < 8.5 (bottom line) indicating impaired cardiac power. An IT may or may not be present.

10. Oxygen Pulse (O_2-Pulse)

Calculated as the ratio VO_2/HR from rest to peak exercise, O_2-pulse represents the volume of O_2 extracted per heartbeat (ml/beat) and is the product of stroke volume and peripheral extraction. The trajectory closely approximates stroke volume pattern during exertion as peripheral extraction is linear and constant during exercise. A low peak O_2-pulse signifies a low peak stroke volume. A plateau or decreasing trajectory past an IT (if present) indicates inducible myocardial dysfunction (IMD). Peak O_2-pulse is an independent predictor of mortality.

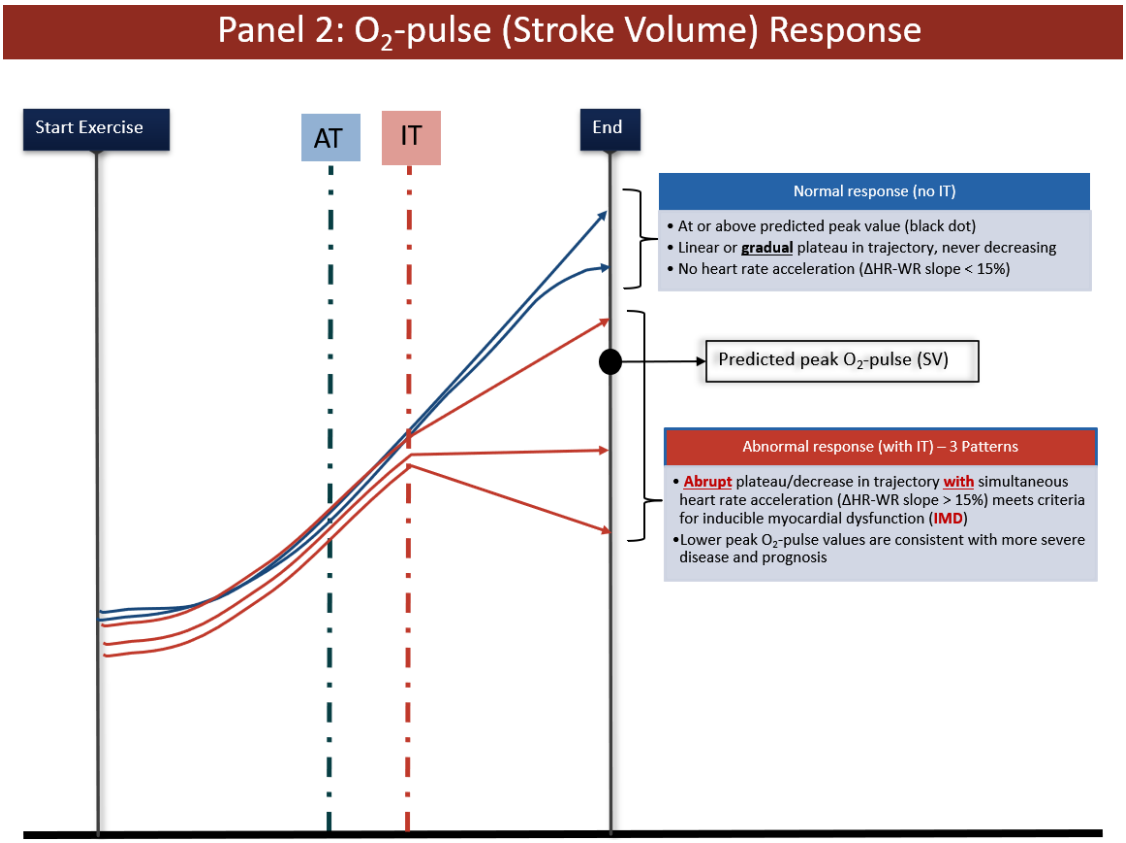
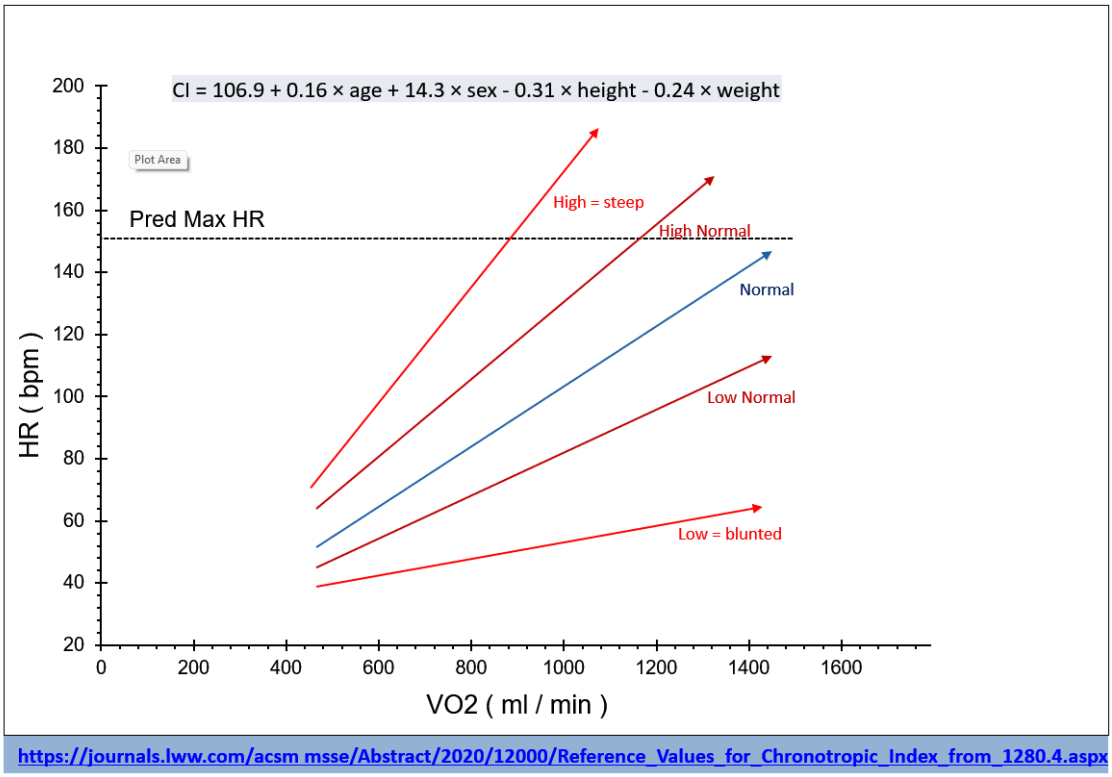


Figure 3 — O_2-Pulse trajectory. Normal: linear rise to peak. Decrease in slope or plateau at IT indicates mild to moderate mechanical dysfunction; decreasing trajectory past IT indicates more severe dysfunction.

11. Heart Rate (HR) Response

Resting HR should be < 90 bpm; a value > 90 is indicative of cardiovascular pathology and is associated with worse prognosis. During exercise, HR increases in a predictable linear fashion. Predicted peak HR = 220 − age. The HR-VO_2 slope (Chronotropic Index, CI) assesses how dependent cardiac output (VO_2) is on HR with increasing workload from start to end. It has established predicted normal values based on age, height, weight, and sex. A steep HR response is pathological and typically seen in cardiomyopathies and valve disorders.

Figure 4: The Chronotropic Index (HR-VO_2 Slope)



https://journals.lww.com/acsm msse/Abstract/2020/12000/Reference_Values_for_Chronotropic_Index_from_1280.4.aspx

Figure 4 — Chronotropic Index (HR-VO_2 Slope) classification. High-steep slopes (red) indicate pathological HR dependence; low-blunted slopes indicate chronotropic incompetence.

Two additional parameters are calculated to determine whether there is HR acceleration in mid-exercise, which is a pathological response to inducible myocardial dysfunction (IMD):

- **ΔHR-WR slope (Panel 2):** ΔHR-WR slope (Panel 2): analyzes the change in HR response in the last 2 minutes of exercise compared to the middle (2 min before AT). In individuals without IMD, this slope stays the same or decreases near peak exercise (ΔHR-WR slope < 15%). In IMD, it abruptly accelerates past the IT in response to mechanical dysfunction (ΔHR-WR slope > +15%), representing a compensatory sympathetic upregulation to maintain cardiac output. A more positive value represents more pronounced compensation.
- **Δ$HR-VO_2$ slope (Panel 3):** Δ$HR-VO_2$ slope (Panel 3): a measure of the change in HR slope in late exercise compared to mid-exercise. After the IT, the $HR-VO_2$ trajectory becomes curvilinear and progressively more positive depending on the degree of compensation. This slope should be zero or negative to represent a normal response; the more positive it is, the more pronounced the change in HR trajectory after the IT. Both serve as diagnostic parameters for IT determination.

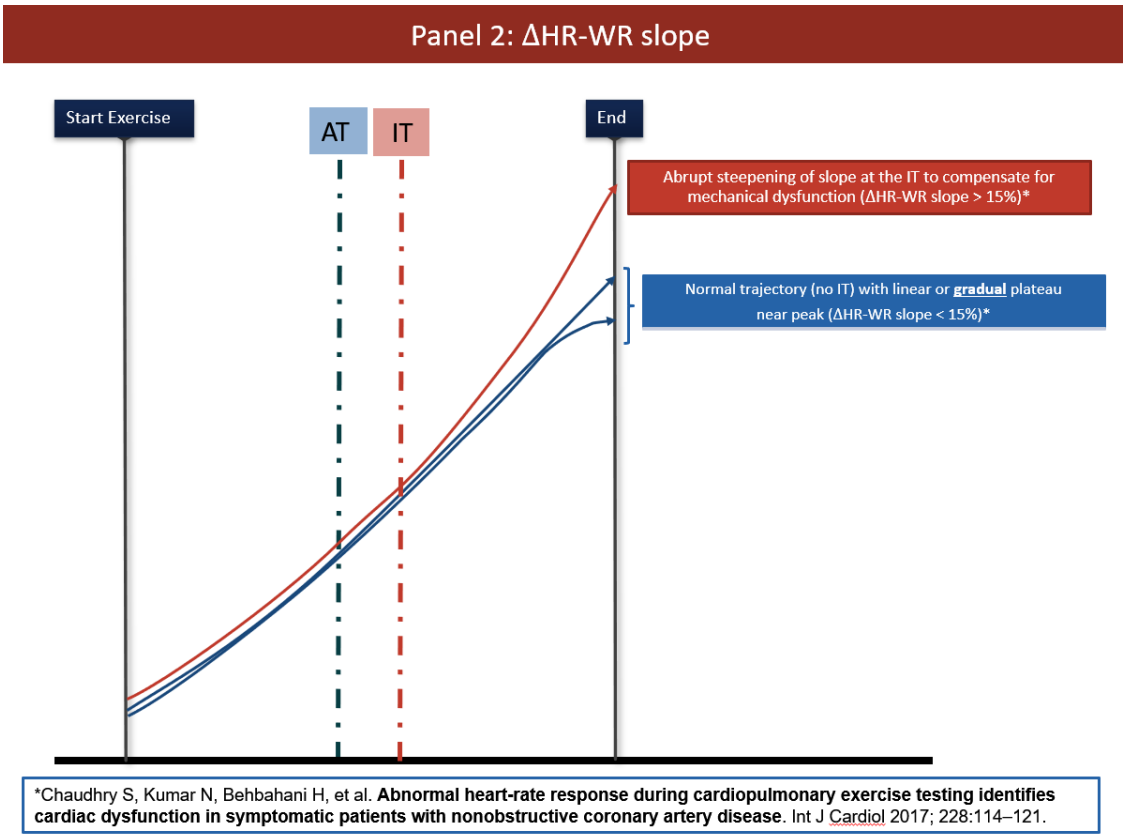


Figure 5 — ΔHR-WR Slope. Normal trajectory (navy) shows linear or gradual plateau. IMD pattern (red dashed) shows abrupt HR acceleration past the IT as stroke volume falls.

12. Blood Pressure (BP) Response

Systolic BP should rise by at least 30 mmHg at peak exercise, normally increasing ~10 mmHg per MET (3.5 mL/kg/min). Diastolic BP does not change or decreases slightly (< 10 mmHg). A rise in diastolic BP ≥ 10 mmHg at peak is pathological and can be seen with cardiac dysfunction.

Published normative data establish predicted peak SBP and SBP/watt slope based on age, height, sex, resting SBP, and peak watts. Women demonstrate lower mean peak SBP than men (188 vs. 202 mmHg) but higher workload-indexed SBP (0.52 vs. 0.41 mmHg/watt). Peak SBP > 110% of predicted warrants more aggressive antihypertensive therapy.

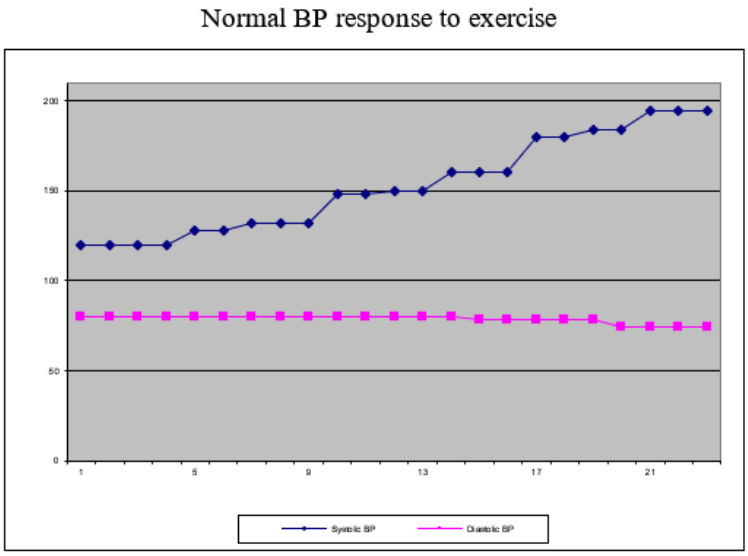


Figure 6a — Blood pressure nomogram during cycle ergometer exercise.

Reference equations and upper/lower limits of normal from:

Hedman K, Lindow T, Elmberg V, Brudin L, Ekström E. *Age- and gender specific upper limits and reference equations for the workload-indexed systolic blood pressure response during bicycle ergometry.* Eur J Prev Card. 2020.

Based on data from 2219 males and 1620 females aged 18-85 years, free from cardiovascular disease, comorbidities and cardiac medications, tested with bicycle ergometry years 2005-2016.

Figure 6b — SBP/watt slope reference values.

13. Stress ECG

ECG tracings obtained during a linear incremental cycle ergometer test are of superior quality to treadmill-based Bruce protocol testing due to reduced motion artifact and more precise reproduction of the ischemic cascade: mechanical dysfunction → electrical ECG changes → clinical symptoms (angina). An ischemic response produces either ventricular ectopy (predominantly PVCs) or ST segment depression in inferior/lateral leads and elevation in right sided leads. Every ECG is precisely analyzed for the exact degree of ST change in all leads with proprietary software. They are categorized as normal, borderline, abnormal and indeterminate. The slopes of the ST changes are also quantified (upsloping vs horizontal). The presence of ST changes has recently been shown to be highly specific for microvascular dysfunction (MVD), with one study revealing 100% specificity. Our algorithms consider borderline changes to be adequate to be considered positive for MVD for this reason. Patients with PVC's have been shown to be 6-10 times more likely to have MVD than patients without.

Pulmonary Parameters

14. Minute Ventilation (VE)

The volume of air inspired and expired in one minute, expressed in liters/min. VE increases in a predictable manner from rest to peak exercise, driven by metabolic demand.

15. Maximum Voluntary Ventilation (MVV)

The upper limit of the body's ability to ventilate the lungs (L/min). MVV is measured directly during pre-exercise spirometry and can be estimated as $FEV_1 \times 40$.

16. Breathing Reserve (BR)

The difference between MVV and ventilation at peak exercise (L/min), representing residual ventilatory capacity remaining at end of exercise. BR < 10% or < 10 L at peak exercise without full cardiovascular stress (peak RER < 1.05) qualifies as ventilatory impairment as the primary mechanism of exercise intolerance.

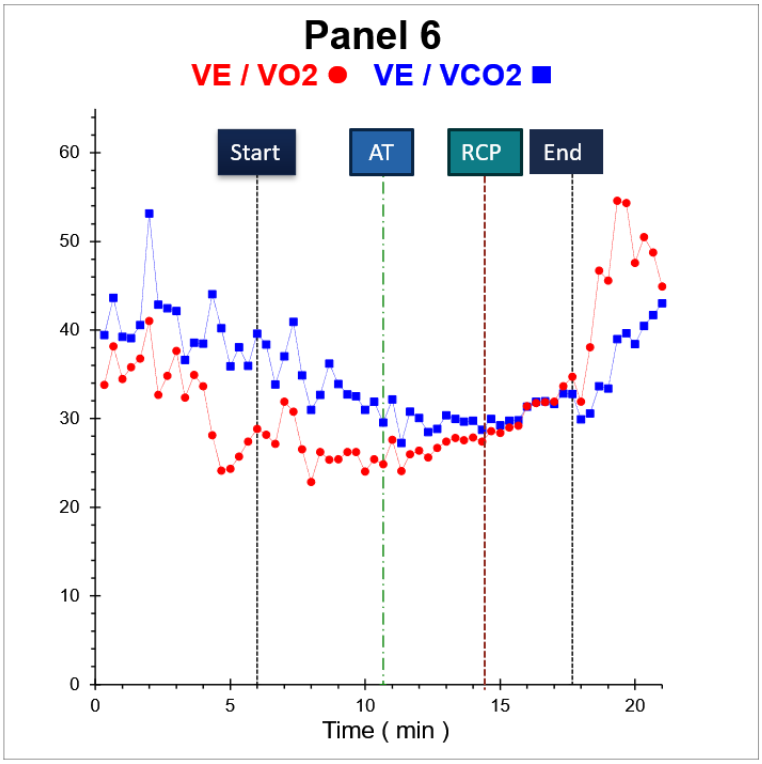
17. Ventilatory Equivalent for CO_2 (VE/VCO_2)

The number of liters of air needed to ventilate the lungs to eliminate one liter of CO_2. A direct measure of gas exchange efficiency and ventilation-perfusion (V/Q) mismatching. Typically measured at the anaerobic threshold (VE/VCO_2@AT). VE/VCO_2 decreases from exercise onset to just past the AT (nadir = respiratory compensation point, RCP), then increases for the remainder of the test.

18. Ventilatory Equivalent for O_2 (VE/VO_2)

The number of liters of air needed to ventilate the lungs to process one liter of oxygen uptake. Also provides a measure of V/Q mismatching. Nadirs at the AT and rises continuously thereafter. With high-quality data, the nadir of VE/VO_2 is an excellent marker for the AT.

Panel 6: Ventilatory equivalents for O_2 and CO_2



Wasserman K, Hansen JE, Sue DY, Stringer WW, Whipp BJ. **Principles of Exercise Testing and Interpretation: Including Pathophysiology and Clinical Applications**, 5th ed, Lippincott Williams and Wilkins, Philadelphia, 2012.

Figure 7 — Ventilatory Equivalents (VE/VCO_2 and VE/VO_2). Both nadir at the anaerobic threshold/RCP. Elevated VE/VCO_2 indicates V/Q mismatching from any cause.

19. VE vs. VCO_2 Slope

The slope of VE (Y-axis, L/min) versus VCO_2 (X-axis, L/min) from rest to the RCP. Higher slopes are a marker of inefficient pulmonary circulation; values greater than the upper limit of normal are considered abnormal.

In heart failure patients, a slope > 35 indicates significant pulmonary congestion from elevated left ventricular diastolic pressures. A slope > 45 strongly indicates primary pulmonary circulation impairment consistent with severe V/Q mismatching. The VE vs. VCO_2 slope is the exercise equivalent of DLCO at rest and is an excellent effort-independent sub-maximal parameter.

20. End-Tidal O_2 and CO_2 ($P_{ET}O_2$ & $P_{ET}CO_2$)

Partial pressure of O_2 and CO_2 in the alveoli at the end of each breath (mmHg). With exercise onset, $P_{ET}O_2$ decreases and $P_{ET}CO_2$ increases up to the AT, then reverses as minute ventilation accelerates.

With V/Q mismatching, resting and early-exercise $P_{ET}O_2$ is elevated and $P_{ET}CO_2$ is reduced due to poor alveolar gas exchange, with minimal change during exertion.

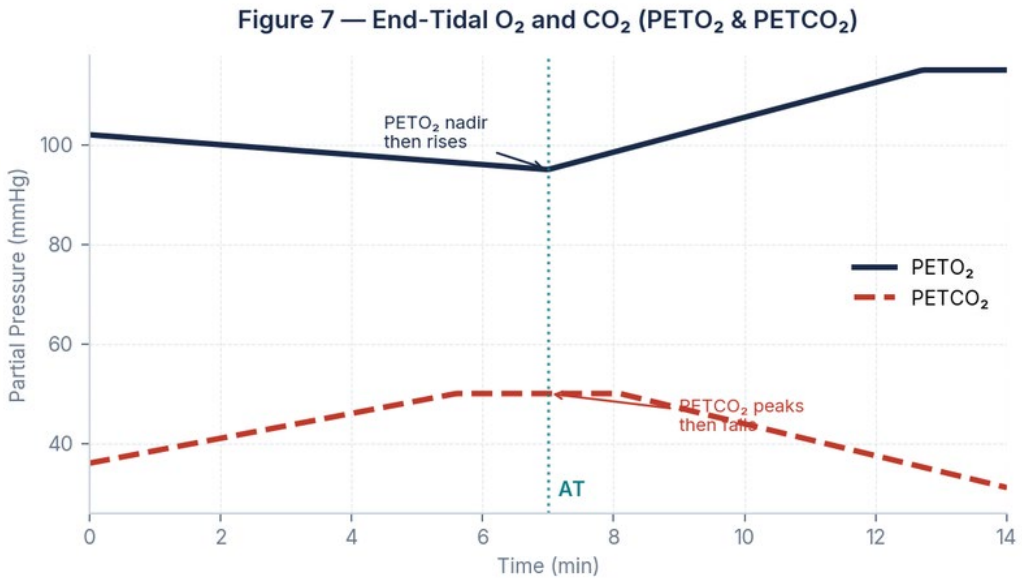


Figure 8 — End-Tidal O_2 ($P_{ET}O_2$) and CO_2 ($P_{ET}CO_2$). $P_{ET}O_2$ nadirs and $P_{ET}CO_2$ peaks at the AT, then both reverse direction as ventilatory drive increases.