Cardiopulmonary Exercise Test: Background, Applicability and Interpretation

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Cardiopulmonary Exercise Test: Background, Applicability and Interpretation

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Abstract

Cardiopulmonary exercise test (CPET) has been gaining importance as a method of functional assessment in Brazil and worldwide. In its most frequent applications, CPET consists in applying a gradually increasing intensity exercise until exhaustion or until the appearance of limiting symptoms and/or signs. The following parameters are measured: ventilation; oxygen consumption (VO₂); carbon dioxide production (VCO₂); and the other variables of conventional exercise testing. In addition, in specific situations, pulse oximetry and flow-volume loops during and after exertion are measured. The CPET provides joint data analysis that allows complete assessment of the cardiovascular, respiratory, muscular and metabolic systems during exertion, being considered gold standard for cardiorespiratory functional assessment.1-6

The CPET allows defining mechanisms related to low functional capacity that can cause symptoms, such as dyspnea, and correlate them with changes in the cardiovascular, pulmonary and skeletal muscle systems. Furthermore, it can be used to provide the prognostic assessment of patients with heart or lung diseases, and in the preoperative period, in addition to aiding in a more careful exercise prescription to healthy subjects, athletes and patients with heart or lung diseases.

Similarly to CPET clinical use, its research also increases, with the publication of several scientific contributions from Brazilian researchers in high-impact journals.

Keywords

Exercise Test; Exercise; Evaluation; Lung Volume Measurements; Oxygen Consumption.

Therefore, this study aimed at providing a comprehensive review on the applicability of CPET to different clinical situations, in addition to serving as a practical guide for the interpretation of that test.

Major variables and their meanings

Oxygen consumption (VO₂): is the volume of O₂ extracted from the air inhaled during pulmonary ventilation in a period of time. It is usually expressed in mL.min⁻¹ or L.min⁻¹ (STPD). In practice, maximum VO₂ (VO₂ max) is defined as the highest value reached, despite progressive increase of the load applied, with the development of a plateau in the VO₂ curve during an incremental exercise test. When no plateau can be identified, the highest value obtained at the end of an exhausting exercise is characterized as peak VO₂, which, in practice, is used as VO₂ max. Mean values at intervals of 10 to 60 seconds should be measured depending on the protocol (short-interval means for protocols with short stages and longer-interval means for protocols with longer stages). The response is influenced by a central mechanism (cardiovascular and/or pulmonary) and peripheral function (skeletal muscle).1-6

The normal values depend on several factors, such as: age, sex, weight, height, physical activity level, genetic variability and ethnicity. Different equations to predict the normal values of VO₂ max or peak VO₂ have been determined from different populations. Although the equation proposed by Wasserman and Whipp⁷ is the most frequently used, a national equation⁸ seems to be more suitable for Brazilians.

The term ‘peak VO₂’ is used as a synonym for VO₂ max throughout this text. Peak VO₂ is considered abnormal when below 85% of the predicted value.⁶ It has been used as a universal marker⁴,5,13 that can broadly reflect disease severity in patients with heart failure (HF), pulmonary hypertension, hypertrophic cardiomyopathy (HCM), chronic obstructive pulmonary disease (COPD) and restrictive pulmonary disease, in addition to physical fitness level.⁴,16 The VO₂ value measured in the first ventilatory threshold (VT1) or anaerobic threshold (AT) is determined by the nonlinear increase of pulmonary ventilation (VE) in relation to VO₂. From the physiological viewpoint, AT represents the upper limit of workloads during exercise, which can be sustained over a prolonged period
of time without progressively increasing blood lactate and consequent pulmonary hyperventilation. Peak VO₂ and AT values are influenced by genetic predisposition, diseases, exercise and aerobic training types. The normal mean AT values expected for adults are around 40% to 65% of peak VO₂. The AT values are important for the individualized prescription of exercise, as well as for the diagnosis of anemia, physical unfitness, myopathies and cardiopathies in the presence of values lower than the predicted ones.  

Pulmonary ventilation (VE): expressed as liters per minute, is the volume of air moved in and out of the lungs. It is determined as the product of respiratory rate by the volume of air exhaled at every cycle (tidal volume). At rest, 7 to 9 L/min are ventilated, but in athletes that value can reach 200 L/min at maximal exertion. Ventilation increases continuously during progressive effort on CPET and undergoes additional increases influenced by the anaerobic metabolism resulting from the accumulation of lactic acid, well defined as the first and second ventilatory thresholds. Periodic (or oscillatory) ventilation is defined as the resting oscillatory pattern that persists in ≥ 60% of the effort with an amplitude ≥ 15% as compared to mean resting values. It reflects disease severity and relates to worse prognosis in patients with HF.  

Respiratory coefficient or respiratory exchange ratio (R): expresses the ratio between CO₂ production and O₂ consumption (VCO₂/VO₂). It is currently the best non-invasive indicator of maximal or quasi-maximal exercise intensity. Values above 1.0 can reflect intense exercise, but those ≥ 1.10 are those searched on CPET, and have been accepted as a parameter of exhaustion or quasi-exhaustion.  

Ventilatory equivalents for oxygen (VE/VO₂) and for carbon dioxide (VE/VCO₂): are the ratios between pulmonary ventilation and O₂ consumption (VE/VO₂) or CO₂ production (VE/VCO₂). Both decline from rest to submaximal exercise intensities, with VE/VO₂ reaching minimum values before AT, when its progressive increase occurs, caused by the increase in ventilation to eliminate extra CO₂ production. That results in lactate buffering by blood bicarbonate. Later, VE/VCO₂ increases (respiratory compensation point - RCP or second ventilatory threshold - VT2), resulting from ventilatory increase (compensatory respiratory alkalosis) in response to blood pH reduction due to the progressive accumulation of lactic acid at muscle level. The VE/VO₂ reflects the ventilatory need for a certain O₂ consumption level, being, thus, an index of ventilatory efficiency. Patients with inadequate ratio between pulmonary ventilation and pulmonary perfusion (increased physiological dead space) ventilate inefficiently and have high VE/VO₂ values (pulmonary disease and HF). Peak values above 50 have been useful to diagnose patients suspected of having mitochondrial myopathy. On the other hand, VE/VCO₂ represents the ventilatory need to eliminate a certain amount of CO₂ produced by active tissues, being influenced by partial pressure of carbon dioxide (PaCO₂). In addition, VE/VCO₂ slope is the relationship between VE, plotted in the Y axis, and VCO₂, plotted in the X axis, both measured as L/min. The VE/VCO₂ slope can be determined in submaximal tests. It relates to changes in the ventilation-perfusion relationship or hyperventilation. The VE/VCO₂ slope reflects the severity and prognosis of patients with HF, pulmonary hypertension, HCM, COPD and restrictive pulmonary disease.  

End-tidal CO₂ partial pressure (PETCO₂): reflects ventilation–perfusion within the pulmonary system, and, indirectly, cardiac function. Its value ranges from 36 to 42 mmHg, with 3- to 8-mmHg elevations during moderate intensity exercise, reaching a maximal value with subsequent drop, due to VE increase, characterizing RCP. Abnormal values can represent disease severity in patients with HF, HCM, pulmonary hypertension, COPD and restrictive pulmonary disease.  

Oxygen pulse (O₂ pulse): is the ratio between VO₂ (mL/min) and heart rate (HR - bpm). Its meaning is better understood by observing the Fick equation: VO₂ = HR x pulmonary volume (SV) x arteriovenous oxygen difference [(A-V)O₂ diff]. Considering that, in many clinical situations, [(A-V)O₂ diff] does not substantially change in incremental exercise, O₂ pulse represents SV and, in a way, left ventricular performance. Thus, VO₂ ≅ HR x SV or VO₂/HR ≅ SV. Under certain circumstances, the morphological analysis of its curve aids in the diagnosis of ventricular dysfunction and important effort-induced myocardial ischemia.  

Breathing reserve (VE/MVV): represents the ratio between maximal ventilation during exercise (VE) and maximum voluntary ventilation (MVV) at rest, both variables in L/min. Equations to predict MVV can be used (forced expiratory volume in the first second – FEV₁, x 40), although it can be measured directly on pre-test spirometry. Normal values are greater than 0.20. However, in both athletes and those performing strenuous exercises, a higher fraction of breathing reserve can be physiologically used. It is useful in the differential diagnosis of dyspnea related to pulmonary mechanism.  

ΔVO₂/ΔWR Relationship: relationship between VO₂ (Y axis in mL.min⁻¹) and workload (X axis in Watts), measured only during exercise on a cycle ergometer with ramp protocol, whose value is progressively and linearly incremented until maximal effort. It is useful in the diagnosis of patients suspected of having myocardial ischemia with left ventricular dysfunction on exertion. Its normal value for adults is 9 mL.min⁻¹.W⁻¹ (the lowest limit being 8.6 mL.min⁻¹.W⁻¹).  

Other variables: the minimum VE/VO₂ value is the cardiorespiratory optimal point (COP). It is a submaximal variable that reflects the best integration between the respiratory and cardiovascular systems. Although it is easy to obtain, further studies are required to determine its clinical applicability and prognostic meaning. Oxygen uptake efficiency slope (OUES) was widely studied, being measured by the relationship between VO₂ and the logarithmic transformation (base 10) of VE. The OUES provides information on the severity of HF. Similarly to VE/VCO₂ slope, it does not require a maximal test. T1/2 VO₂ is the time necessary for a 50% drop in VO₂ measured at peak exercise (from the beginning of recovery) until the third minute of recovery. It decreases with physical training and its increase is negatively associated with the prognosis of HF patients. Circulatory power is the product of peak systolic blood pressure (SBP) by peak VO₂ while ventilatory power is peak SBP divided by VE/VCO₂ slope. Both have prognostic value in HF. Finally, the association of CPET with measurements of...
Functional assessment and CPET-based aerobic exercise prescription

The CPET is considered the best method to assess aerobic performance, and, mainly, to support aerobic exercise prescription. Considered class IIa indication - optimized prescription of exercise to healthy individuals, individuals with heart or lung diseases entering a program of regular exercise - and class IIb indication – athletes - it is still rarely used with such purposes by clinical cardiologists.

By use of the joint analysis of exhaled gases, work and/or exertion performed and the behavior of hemodynamic variables, mainly HR, a more comprehensive functional assessment can be obtained. Thus, a more precise and individualized program of aerobic exercise can be outlined. Apparently healthy individuals who engage in moderate- to high-intensity aerobic practice can benefit from CPET regarding exercise prescription and performance assessment.

For individuals with heart diseases and high-performance athletes, such benefits have been widely established. Prescription errors, both insufficiency and excess, in such individuals can have a negative impact on the results expected from a training program.

Briefly, for the prescription of aerobic exercises, the most relevant data obtained from CPET are HR and exercise intensity at which the ventilatory thresholds occur, especially, AT or VT1. The exercise intensity at which VT1 occurs characterizes the highest submaximal level tolerated by a certain individual for long time periods. Because that exercise intensity varies even between two individuals with identical maximal functional capacity (and even with similar maximal VO2 values measured), its precise determination via CPET enhances and refines the quality of aerobic exercise prescription. In practical terms, HR values in different points of maximal CPET are used to establish the bases for a more objective prescription. More often, the following values are considered: HR at rest with the individual lying down (resting HR), maximal HR (HRmax), HR at AT, HR at RCP, and HR at the ‘R = 1’ point. Traditionally, exercises have been prescribed based on the intensity related to HR, but the workload related to thresholds and maximal effort can also be used. When the objective is to train up to a moderate subjective intensity that can be sustained for long periods, we set the limit at the AT. Between the AT and RCP, the exercise intensity is higher, but usually still tolerated for prolonged periods, with wide individual variations. Finally, the training can be performed above the RCP, with very intense and much more difficult to sustain exercises, which can be of the interval type (alternating resting periods with some type of mild-to-moderate intensity exercise).

There are numerous protocols that can be used for both healthy individuals and those with diverse pathologies. These protocols are used to prescribe steady-state aerobic exercise (walking or running) or interval exercise, with an important component of “anaerobic” exercise, alternating rhythms and intensities (alternate walking and running, up and down walking and cycling, ball sports and spinning classes).

However, the quality of that prescription, based on HR derived from CPET, depends on some factors. It is convenient that CPET be performed with a ramp protocol, minimum duration of eight minutes, on an ergometer more similar to the aerobic exercise that will be prescribed (cycle ergometer for cyclers, treadmill for runners). Longer protocols tend to allow greater differentiation and precision in identifying the exercise intensity that corresponds to the thresholds. It is worth noting that data collected during a CPET performed in an air-conditioned room can differ from those obtained during a walk or cycling or even a long running (more than 45 minutes) at open air locations and under more adverse climate conditions, in which there may be a cardiovascular drift phenomenon, characterized by a progressive increase of HR, instead of remaining in steady-state, despite of a constant intensity of exercise. However, for patients using HR-controlling devices or on regular use of medications with negative chronotropic action, specific care should be taken so that the HR-based prescription obtained on CPET can remain valid. The most obvious case is that of patients on beta-blockers on a single daily dose, which make HR during exercise vary according to the time interval between medication administration and exercise performance. To minimize that chronopharmacological effect, such patients should undergo CPET at the time closest to that of regular exercise. In patients with pacemakers, resynchronization devices and atrial fibrillation, the HR measured by these HR sensors is inaccurate. For those individuals and some athletes whose training intensity is based on load or velocity, exercise can be prescribed based on velocities or loads relative to thresholds. Some studies have suggested that the load relative to ‘R = 1’ bears the best correlation with maximal exertion in metabolic balance.

Finally, other potentially relevant variables can be obtained via exhaled breath analysis, including some that do not require maximal exertion, such as mechanical efficiency analysis and CO2 which widens the CPET value for prescription of primarily aerobic exercises.

CPET in heart failure

Chronic heart failure (CHF) is a systemic syndrome, and reduced functional capacity is one of its main features. The cardiovascular deficit has a direct influence on other organs and systems, such as the pulmonary, renal and skeletal muscular ones. CPET is considered “gold standard” for the functional assessment of patients with CHF, propitiating diagnostic and prognostic data derived from direct measurement of VO2, VCO2 and VE. In addition, the variables VE/VO2, VE/VCO2, VCO2/VO2 and R, as well as the metabolic points AT and RCT, are useful parameters to indicate accurately the maximal aerobic capacity, to quantify functional restriction, to measure the response to drug therapy and to guide physical training prescription.

The Brazilian Society of Cardiology guidelines for the management of patients with CHF present CPET as class I
indication in the assessment of both heart transplantation candidates and dyspnea mechanisms. The use of CPET is class II indication for exercise prescription, and to assess the severity, prognosis and responses to therapeutic interventions in CHF.2,26

The response to CPET of a patient with CHF is characterized by: reduced VO$_2$ p.AT $< 40\%$ of the predicted VO$_2$ max, O$_2$ pulse $< 85\%$ and as a plateau, increased VE/VCO$_2$, reduced OUES, wide breathing reserve and usually normal O$_2$ saturation.2 Peak VO$_2$ is the specific and direct measure of functional capacity. Several studies have shown its independent prognostic capacity in CHF. According to the Brazilian guidelines for heart transplantation, a peak VO$_2$ lower than 10 mL.kg$^{-1}$.min$^{-1}$ is class I indication for that procedure, while a peak VO$_2$ below 12 mL.kg$^{-1}$.min$^{-1}$ (patients on beta-blocker) or below 14 mL.kg$^{-1}$.min$^{-1}$, is class IIa indication, particularly for those with other criteria of worse prognosis (VE/VCO$_2$ slope $> 35$).27 Weber et al.28 have proposed a classification for peak VO$_2$ results: class A = VO$_2$ $> 20$ mL.kg$^{-1}$.min$^{-1}$; class B = VO$_2$ 16-20 mL.kg$^{-1}$.min$^{-1}$; class C = VO$_2$ 10-15 mL.kg$^{-1}$.min$^{-1}$; and class D = VO$_2$ $< 10$ mL.kg$^{-1}$.min$^{-1}$. It is worth noting that, for peak VO$_2$ value to have prognostic accuracy, the test has to meet the requirements of a maximal test (proposed for HF: R $> 1.05$, at least).

Other important variables measured via CPET that add independent prognostic value for patients with CHF are: VE/VCO$_2$ slope, OUES, T$_{1/2}$VO$_2$, HR recovery in the first post-exertion minute, presence of periodic ventilation, and PETCO$_2$ and O$_2$ pulse behaviors.

Chua et al.29 assessing patients with CHF using CPET, have observed those with VE/VCO$_2$ slope $> 34$ were at higher risk for hospitalization due to decompensation, and for death. Other authors,30-32 assessing the prognostic value of VE/VCO$_2$ slope in CHF, have shown it to be a variable with excellent independent value, even higher than that of peak VO$_2$, and important to patients who reach only submaximal exertion. In a population with CHF due to Chagas disease, Ritt et al.31 have reported that the best cutoff point for worse prognosis was VE/VCO$_2$ slope $> 32.5$, thus earlier than those reported by studies on other etiologies. Arena et al.34 have published the following ventilatory classes based on VE/VCO$_2$ slope values: class I, VE/VCO$_2$ $\leq 29.9$; class II, 30-35.9; class III, 36-44.9; class IV $\geq 45$. In 2 years, event-free survivals (death, transplantation or implantation of ventricular assistance device) for classes I-IV were 97.2%, 85.2%, 72.3% and 44.2%, respectively (P $< 0.0001$). Assessing a population of patients via CPET for heart transplantation, Ferreira et al.35 have found a VE/CO$_2$ slope cutoff point of $\geq 43$ as ideal to determine the indication for heart transplantation. The use of VE/VCO$_2$ slope as a criterion for selection of candidates for transplantation could reclassify correctly 18.3% more patients than the classic peak-VO$_2$-based criteria (p $< 0.001$).31

In addition, OUES has an independent prognostic value. Initially, Baba et al.36 have described that variable behavior, whose cutoff point and independent prognostic value were subsequently assessed by other authors. A cutoff point $< 1.47$ L/min determines a group with more severe CHF.37,34 T$_{1/2}$VO$_2$ is identified in patients with CHF. Studying patients with VO$_2$ $\geq 15$, between 10.1 and 14.9, and $\leq 10$ mL.kg$^{-1}$.min$^{-1}$, Groote et al.38 have reported T$_{1/2}$VO$_2$ values of 108 $\pm$ 44.6, 137 $\pm$ 58.7, and 176 $\pm$ 75 seconds, respectively.38 In patients with no heart disease, T$_{1/2}$VO$_2$ is usually $< 90$ seconds.39

The kinetics of HR recovery (HRR) is a well-established prognostic marker in patients with CAD,40 related to changes in post-exertion autonomic balance. In CHF, it is also an independent factor of mortality, even in patients on beta-blockers.41 The cutoff point established for that population was $\leq 16$ bpm in an active recovery protocol (hazard ratio: 4.6; 95%CI: 2.8-7.5; p $< 0.001$). Its clinical usefulness has been assessed for heart transplantation indication in patients in the intermediary zone of peak VO$_2$ (VO$_2$ 10.1-13.9 mL.kg$^{-1}$.min$^{-1}$), in whom, the HRR analysis aggregated value to peak VO$_2$ and VE/VCO$_2$ slope. The prognosis of patients with altered HRR and VE/VCO$_2$ slope was comparable to that of those with VO$_2$ $< 10$ mL.kg$^{-1}$.min$^{-1}$.42

Wide oscillations in ventilation during exertion relates to cardiovascular events and death in patients with CHF. That pattern, analogous to the Cheyne-Stokes respiration, was named periodic ventilation. The occurrence of periodic ventilation during exertion (characterized by an amplitude variation $> 5$ L/min for at least three cycles) was related to an up to three-fold higher mortality in patients with CHF (hazard ratio: 2.97; 95%CI: 1.34 – 6.54; p $< 0.007$).43,44 The presence of periodic ventilation increased the risk of patients with reduced peak VO$_2$ and elevated VE/VCO$_2$ slope.45

Another index that reflects the dynamics of pulmonary changes and CO$_2$ diffusion at alveolar level is PETCO$_2$ at rest. Mean values $< 33$ mmHg after 2 minutes at rest were independently correlated with worse prognosis and greater mortality in CHF (hazard ratio: 2.17; 95%CI: 1.48-3.19; p $< 0.001$).46

O$_2$ pulse can be assessed regarding its absolute value and its behavior during exertion. A plateau is usually related to an insufficient increase in SV on exertion. An O$_2$ pulse $< 85\%$ of the predicted value correlates independently with major cardiovascular events in CHF. Among patients with peak VO$_2$ $< 14.3$ mL.kg$^{-1}$.min$^{-1}$ and O$_2$ pulse $< 85\%$ of the predicted values, mortality was greater than among those with only one of those parameters altered (hazard ratio: 4.76 versus 2.31, respectively). O$_2$ pulse could also reclassify the risk of patients into intermediate zone of peak VO$_2$ for transplantation (10-14 mL.kg$^{-1}$.min$^{-1}$). Patients in the O$_2$ pulse $< 85\%$ zone had mortality similar to those with VO$_2$ $< 10$ mL.kg$^{-1}$.min$^{-1}$.47

Each CPET variable correlates with the interaction of HF with another organ or system. Thus, the joint analysis of those variables can better stratify the risk of those patients. The CPET variables can be combined into risk scores in CHF. Levy et al. have shown that the addition of VE/VCO$_2$ slope data to Seattle Heart Failure Model could improve the prognostic ability of that score, reclassifying 40% of the patients into a more appropriate risk category (p = 0.002).48

To determine the prognostic significance of CPET in CHF, Cahalin et al. have conducted a meta-analysis of studies
published until 2013 and calculated the odds ratios (OR) of each prognostic variable. The OR of the main prognostic variables assessed (peak VO$_2$, VE/VCO$_2$, slope, OUES and periodic ventilation) were 4.10 (CI: 3.16–5.33), 5.40 (CI: 4.17–6.99), 8.08 (CI: 4.19–15.58) and 5.48 (CI: 3.82–7.86), respectively.  

For those not dealing with CPET on a daily basis, the assessment of each variable can be unpractical. Myers et al. have developed a score that combines the information of the main CPET variables into a number. The points are attributed as follows: VE/VCO$_2$ slope ≥ 34 - 7 points; HRR ≤ 16 bpm - 5 points; OUES ≤ 1.4 - 3 points; PETCO$_2$ < 33 mmHg - 3 points; peak VO$_2$ ≤ 14 mL·kg$^{-1}$·min$^{-1}$ - 2 points. The score ranges from 0 to 20, 0-5 being the reference. The others correlated in an increasing manner with the risk of death/transplantation or implantation of ventricular assistance device: 6-10 (hazard ratio: 2.74, 95%CI: 2.16–3.48; p < 0.001), 11-15 (hazard ratio: 4.6, 95%CI: 3.55–5.98; p < 0.001) and > 15 (hazard ratio: 9.25, 95%CI: 5.75–14.88; p < 0.001). In three years, the mortality of patients with score > 15 was 12.2%, in comparison to 1.2% in those with score < 5. A recent analysis applied that score to class B patients according to Weber heart failure classification (analogous to NYHA class II). In the three-year follow-up, patients with score ≥ 10 had an event-free survival equivalent to that of Weber class C patients, and those with score < 10 had a prognosis equivalent to that of Weber class A patients.

The CPET plays a preponderant role in the assessment of patients with CHF, not only regarding the selection of candidates for transplantation, but also to determine the prognosis and help with the therapeutic decision. Figure 1 shows a stratification strategy that combines those variables.

**CPET to assess myocardial ischemia**

CPET can help to assess myocardial ischemia in patients with suspected CAD, a clinical condition where a significant ischemic load, during exercise, is expected to negatively influence systolic myocardial performance. During incremental exercise, the myocardial unbalance between O$_2$ offer and demand triggers a sequence of metabolic changes that can ultimately lead to the insufficient physiological elevation of SV. On CPET, this is observed as a depressed, in plateau or declining shape curve of O$_2$ pulse.

Three CPET variables are indicated to assess the presence and severity of myocardial ischemia: 1) O$_2$ pulse; 2) VO$_2$ curve and elevation; and 3) relationship between VO$_2$ variation and load variation, in watts, in this case, exclusively, on cycle ergometer.

**Oxygen pulse and oxygen consumption curve**

Usually, (A-V)O$_2$ diff tends to remain constant during incremental exertion, except for rare cases of anemias,
hemoglobinopathies, some congenital heart diseases and COPD, in which there is a significant drop in peripheral oxygen saturation. Except for those clinical conditions, one can infer that SV behavior during incremental exercise is reflected by the equation: \( \frac{V_O}{HR} = SV \). The \( \frac{V_O}{HR} \) ratio, called “oxygen pulse” and measured in milliliters per beat, reflects the \( O_2 \) volume ejected into the aorta at every systole. Likewise, \( SV \), also measured in milliliters per beat, reveals the blood volume ejected into the aorta at every systole. Thus, those two variables, despite being numerically different, reflect left ventricular hemodynamic behavior during CPET.

The analysis of the \( \frac{V_O}{HR} \) curve as a function of time, which should have the increasing morphology of a parabola, is as important as the numerical \( O_2 \) pulse value during the incremental phase of CPET. The identification of a curve with a plateau or decline indicates a reduction in \( O_2 \) pulse and \( SV \) during exercise, and can indicate myocardial ischemia (Figure 2). It is worth noting that other clinical conditions can cause similar changes, such as ventricular dysfunctions due to non-ischemic cardiomyopathies, providing prognostic information on HF with reduced ejection fraction, and obstructive valve heart diseases. In the presence of severe chronotropic changes, artificial electric stimulation and arrhythmias, such as atrial fibrillation, \( O_2 \) pulse analysis becomes compromised and inaccurate.

**\( \Delta V_O/\Delta WR \) Ratio (Watts)**

To every increase in load imposed during CPET, a similar increase in \( V_O \) is expected. Normally, a 1-Watt increment in workload should correspond to a 10 mL.min\(^{-1}\)-increase in absolute \( V_O \). The loss of this linear relationship, with a reduction of slope often to less than 5 mL.min\(^{-1}\).Watt\(^{-1}\), despite the increase in exercise intensity during CPET, contributes to the diagnosis of myocardial ischemia (Figure 3).

It is worth noting that the changes suggestive of ischemia on CPET become more evident as ischemia severity increases. The CPET variables should be analyzed in light of the pre-test clinical suspicion. CPET can be indicated for functional assessment of patients with established CAD, as well as for the investigation of myocardial ischemia diagnosis, mainly in the following conditions:

1. When there is moderate to high pre-test likelihood of myocardial ischemia;
2. To increase diagnostic accuracy of myocardial ischemia, when, on CPET, there is clinical, hemodynamic or electrocardiographic change, hindering the diagnosis via conventional exercise test;
3. In the presence of a large ischemic myocardial area, hindering left ventricular function due to \( SV \) reduction during exercise;
4. For follow-up assessment after percutaneous or surgical revascularization;
5. Similarly to other clinical conditions, CPET can be recommended to assess the prognosis of patients with CAD with or without evidence of ischemia, by using other variables usually used for that purpose, such as \( VE/VCO_2 \) slope, peak \( V_O \), OUES, periodic ventilation and \( T_1/2\ V_O \).

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**Figure 2** – Cardiopulmonary exercise test in the pre-rehabilitation assessment of a 57-year-old hypertensive, diabetic, overweight male patient with three-vessel coronary disease, who refused to undergo myocardial revascularization surgery eight years earlier. A) evident drop in oxygen pulse. B) early plateau of oxygen consumption. Both changes (A and B) were due to ischemic depression of the ST segment (evident in A), followed by progressive chest pain.
Figure 3 – The $\Delta VO_2/\Delta WR$ relationship around 10mL.min.Watts suddenly reduces, despite the exercise intensity increase. This loss of linear relationship could indicate the presence of myocardial ischemia by use of CPET performed on a cycle ergometer (modified from reference 52).

in addition to other CPET variables that wait for more solid studies. 6,54-57

**CPET in the differential diagnosis of dyspnea**

Dyspnea is a common symptom in several clinical situations, characterized by the perception of respiratory difficulty or discomfort. Its pathophysiology is complex, involving neuro-humoral and mechanical mechanisms. From the practical viewpoint, the differential diagnosis can be classified into four categories: cardiac, pulmonary, mixed cardiopulmonary, and non-cardiopulmonary. 58,59

The use of CPET for dyspnea assessment can be divided into two settings - patients with dyspnea without an established diagnosis and patients with multiple possible causes - in whom the test is useful to determine which mechanism prevails and causes symptoms. The dyspnea, whose cause cannot be elucidated via history, physical examination and complementary tests at rest, should be better assessed by using CPET. By use of joint analysis, from rest to maximal exertion, the cardiovascular, respiratory and peripheral metabolism responses can provide information on the dyspnea mechanism. Because of its low cost, CPET can be indicated early in the investigative hierarchy of dyspnea assessment, serving to guide other complementary tests, when required, for therapeutic management and prognostic assessment (Table 1).

Studies on the clinical value of CPET in patients with chronic dyspnea (more than 1 month) of undetermined origin or dyspnea of multiple causes have evidenced practical use: to differentiate dyspnea of cardiocirculatory primary origin from dyspnea of pulmonary ventilatory etiology or that related to problems in the ventilation-perfusion binomial; to quantify the different mechanisms of multiple-cause dyspnea; to identify an unsuspected or underestimated circulatory component; and to identify a psychogenic or simulation component. 60,61

The differential diagnosis of those pathologies requires pragmatic interpretation of CPET data. 62 The first step is to assess peak $VO_2$ and to determine the percentage of the predicted value achieved. Pulmonary, cardiovascular and metabolic diseases or physical unfitness can account for $VO_2$ reduction. Then, breathing reserve should be assessed, and, when low, it can identify underlying pulmonary disease. Breathing reserve lower than 20% is found in pulmonary diseases; however, as already described, highly-trained individuals or those in situations of extreme exertion can also consume their ventilatory reserve on maximal exertion as a compensatory mechanism, but, in such cases, peak $VO_2$ will not be significantly reduced.

The following step is the analysis of $O_2$ saturation. A drop greater than 4% on peak exertion as compared to resting is characteristic of pulmonary limitation. High $VE/VCO_2$ slope and $PETCO_2 < 33 mmHg$ at rest and/or elevation greater than 8 mmHg during exertion suggest respiratory mechanisms as the cause of dyspnea. 3,63

Observation of $O_2$ pulse and $\Delta VO_2/\Delta WR$ ratio can identify heart disease, if the curves show plateau or decline, reflecting
Table 1 – Behavior of major CPET variables in several causes of dyspnea

<table>
<thead>
<tr>
<th>Dyspnea origin</th>
<th>Cardiovascular</th>
<th>Pulmonary</th>
<th>Vascular-pulmonary</th>
<th>Hyperventilation</th>
<th>Fake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO₂</td>
<td>reduced</td>
<td>reduced</td>
<td>reduced</td>
<td>normal</td>
<td>reduced</td>
</tr>
<tr>
<td>AT</td>
<td>early</td>
<td>normal</td>
<td>early</td>
<td>normal</td>
<td>normal</td>
</tr>
<tr>
<td>R</td>
<td>normal</td>
<td>reduced</td>
<td>normal/reduced</td>
<td>normal/reduced</td>
<td>reduced</td>
</tr>
<tr>
<td>VE/VO₂ slope</td>
<td>high</td>
<td>high</td>
<td>high</td>
<td>high</td>
<td>normal</td>
</tr>
<tr>
<td>PETCO₂</td>
<td>low</td>
<td>low</td>
<td>low at AT</td>
<td>low at AT</td>
<td>normal</td>
</tr>
<tr>
<td>VE/MVV</td>
<td>normal</td>
<td>reduced</td>
<td>normal</td>
<td>normal</td>
<td>normal</td>
</tr>
<tr>
<td>O₂ pulse</td>
<td>reduced/plateau</td>
<td>normal/plateau</td>
<td>reduced/plateau</td>
<td>normal</td>
<td>normal</td>
</tr>
<tr>
<td>O₂ Sat</td>
<td>normal</td>
<td>drop</td>
<td>drop</td>
<td>drop</td>
<td>normal</td>
</tr>
<tr>
<td>ΔVO₂/ΔWR</td>
<td>reduced/plateau</td>
<td>normal/plateau</td>
<td>reduced/plateau</td>
<td>normal</td>
<td>normal</td>
</tr>
</tbody>
</table>

VO₂: oxygen consumption; AT: anaerobic threshold; VE/VO₂ slope: ratio between pulmonary ventilation and carbon dioxide production; PETCO₂: extrapolated end-tidal carbon dioxide tension; VE/MVV: ventilatory reserve; O₂ Sat: oxyhemoglobin saturation; ΔVO₂/ΔWR: relationship between oxygen consumption and workload.

an inadequate SV to the load imposed. However, individuals with lung disease and some degree of pulmonary hypertension can also develop a plateau of O₂ pulse. The combination of plateau of O₂ pulse with a decrease in O₂ saturation, VE/VO₂ slope > 40 and reduced PETCO₂ (< 33 mmHg at rest or < 36 mmHg at AT) strongly suggests pulmonary hypertension or a pathology with pulmonary vascular impairment.

Patients with dyspnea due to cardiovascular limitation have reduced VO₂, early AT, ventilatory inefficiency (high VE/VO₂ slope), inefficient O₂ uptake (reduced OUES), plateau of O₂ pulse or of ΔVO₂/ΔWR ratio, with normal ventilatory reserve, PETCO₂ < 33 mmHg at rest and/or increase < 3 mmHg during exertion, in addition to lack of drop in O₂ saturation.

Patients with physical unfitness and anemia have reduced VO₂ and increased ΔVO₂/ΔWR (cycle ergometer), but they do not meet the criteria for pulmonary or cardiovascular limitation. Extremely physically unfit patients can have reduced AT and increased HR/VO₂ ratio. On the other hand, a low R, despite the sensation of extreme fatigue on BORG scale, points to a peripheral mechanism as the cause of limitation to exertion.

Patients with hyperventilation have reduced ventilatory efficiency (high VE/VO₂ slope), reduced PETCO₂ at AT, sudden changes in the ventilatory pattern with phases of tachypnea and hypopnea, and extremely increased respiratory rate on exertion. Usually, the ventilatory reserve is normal and O₂ saturation has a physiological behavior.

Studying 39 patients with asthma of difficult control, McNicholl et al. have reported that, in 14 of them, the persistent complaint of dyspnea was explained by hyperventilation, preventing the undue increase of the dose of bronchodilators in those patients. In legal situations, facing a complaint of dyspnea, the medical expert can have difficulty to determine if the symptom is true or to establish an effective symptom graduation, and CPET can be used to clarify the scenario. To diagnose fake dyspnea by using CPET: the patient reports extreme fatigue, asks for exertion interruption and shows normal ventilatory reserve, normal O₂ saturation behavior, AT within the expected range for the maximal VO₂ predicted (40%-60%), but an R compatible with submaximal exertion (<1), in addition to apparent chronotropic deficit.

**CPET in pulmonary diseases**

**Chronic obstructive pulmonary disease**

The severity of COPD is determined based on symptoms and spirometry results. Pulmonary function tests at rest, however, do not accurately predict the grade of intolerance to exertion. The inability to increase ventilation to levels that allow high gas exchange is one of the mechanisms that explain dyspnea on exertion. That phenomenon can be observed on CPET and is usually interpreted as ventilatory limitation. Although characteristic of obstructive scenarios, it can occur in restrictive diseases, such as interstitial pulmonary diseases, and in abnormalities of the thoracic cage. The criterion that defines ventilatory limitation is arguable, but, when the breathing reserve at peak exertion is lower than 15%, limitation is considered to occur, especially when R is lower than 1.0.

In patients with COPD, peak VO₂ continues to be the best index of aerobic capacity, as long as patients exercise to their limit. However, other aspects should be considered when interpreting the CPET of patients with COPD. There is a combination of low ventilatory capacity and high ventilatory demand, increasing the sensation of dyspnea. The perception of lower limb exertion is often exaggerated in such patients and can be a limiting factor, especially in tests performed on a cycle ergometer. Another factor that can significantly contribute to the development of unbearable dyspnea during exercise is dynamic hyperinflation. With the increase of respiratory flow during exercise, the air is held in the lungs, causing a progressive increase in residual volume, thus reducing the inspiratory capacity (Figure 4). That frequently occurs together with a
Reduction in tidal volume, indicating that the respiratory mechanics has reached its functional limit. Dynamic hyperinflation can be observed on CPET when periodic analyses of the flow-volume curve occurs with inspiratory capacity measured during exercise. That is especially useful when symptom intensity and the grade of airway obstruction is disproportional.

Exertion-induced bronchospasm

Exertion-induced bronchospasm (EIB) is the acute narrowing of airways resulting from exercise. Its clinical manifestations include “chest wheezing”, cough, dyspnea or chest pressure usually 5 to 10 minutes after exercise, and, less commonly, during exercise. Its diagnosis requires a specific protocol with repeated post-exertion spirometry, typically at 5, 10 and 15 minutes. A drop in FEV1 equal to or greater than 10% as compared to that of pre-exertion is diagnosed as EIB. For the diagnosis of bronchial hyperreactivity, that test is less sensitive than bronchoprovocation challenge tests with bronchoconstrictors (methacholine, histamine), being, however, more specific for the diagnosis of EIB.

Early detection of pulmonary vascular disease

In addition, CPET has been used to the early detection of pulmonary vascular disease. However, the pathophysiological aspects of pulmonary hypertension are worth considering to understand and interpret the findings in the clinical context.

Pulmonary hypertension is defined as mean pulmonary artery pressure (mPAP) equal to or greater than 25 mmHg, and dyspnea on exertion is usually its earliest symptom. The pulmonary circulation has high capacitance, and normal mPAP values are frequently observed at the early...
stages of pulmonary vascular disease. For an increase in mPAP levels at rest to occur, more than 50% of the pulmonary circulation needs to be obstructed, resulting in a relatively late diagnosis of pulmonary vascular disease.

The identification of pulmonary hypertension during exertion requires the use of a pulmonary artery catheter for direct measurement during exercise. This is part of the invasive (or advanced) CPET, available only at a few centers. One limitation is that the definition of pulmonary hypertension on exertion, mPAP greater than 30 mmHg, is arbitrary, and healthy individuals can reach much higher values. In addition, there are not enough data to conclude that patients with that “abnormal hemodynamics” will progress to true pulmonary hypertension at rest.

CPET can provide information to help the clinician suspect pulmonary hypertension when assessing a patient with dyspnea of undefined etiology. The VE/VCO₂ ratio at AT and peak exertion are extremely elevated in patients with pulmonary hypertension, higher than that of patients with HF and same functional class. In addition, low PETCO₂ values at the end of expiration, both at rest and exercise, were associated with pulmonary hypertension.

It has been suggested that, in the absence of acute hyperventilation (normal R), VE/VCO₂ ratio greater than 37 and PETCO₂ below 30 mmHg at AT could indicate pulmonary vascular disease. Exceptionally low PETCO₂ values (below 20 mmHg) are uncommon in other diseases and increase the suspicion of pulmonary hypertension in patients assessed for dyspnea on exertion.

Prognostic assessment in pulmonary hypertension

CPET can be used to assess both the severity of pulmonary hypertension in patients with established disease and the response to therapy. Studying idiopathic pulmonary arterial hypertension, Wensel et al. showed that individuals with peak VO₂ lower than 10.4 mL.kg⁻¹.min⁻¹ and peak SBP lower than 120 mmHg had worse prognosis. The guidelines of the European Society of Cardiology recommend that peak VO₂ values greater than 15.0 and lower than 12.0 mL.kg⁻¹.min⁻¹ indicate good and bad prognosis, respectively. However, that parameter should not be assessed isolated, but be part of a comprehensive assessment to determine pulmonary hypertension severity.

In addition, VE/VCO₂ ratio at AT and VE/VCO₂ slope have been associated with pulmonary hypertension prognosis, with values equal to or greater than 54 and 62, respectively, indicating shorter survival. However, that relationship seems not to apply to all forms of pulmonary hypertension. A more elevated VE/VCO₂ slope was observed in pulmonary hypertension due to chronic pulmonary thromboembolism as compared to pulmonary arterial hypertension. It is worth noting that, in pulmonary hypertension due to chronic pulmonary thromboembolism, VE/VCO₂ slope did not associate with functional class, suggesting no relationship with severity and high values at early phases. Another parameter associated with the worse survival of patients with pulmonary arterial hypertension is the presence, on CPET, of signs of right-to-left shunt during exercise.

Figure 4: Flow-volume curves: A) patient without pulmonary disease; B) patient with chronic obstructive pulmonary disease. Note loop displacement to the left with overlapping.

CPET in children and adolescents

In the pediatric population, the use of CPET is similar to that of the adult population, but with specific particularities related to the childhood universe. Environmental conditions should allow children to adapt to the test, therefore enabling good performance assessment.

CPET has been very useful to assess healthy individuals and those with complex congenital heart diseases, allowing the determination of pathophysiological causes that limit functional capacity. Protocols and ergometers (treadmill and cycle ergometer) are selected according to the objectives and experience of the laboratories conducting the tests. Ramp protocols, however, are currently the most often applied.

Comparing the cardiorespiratory responses of healthy children with those of healthy young adults, Prado et al. have evidenced lower cardiovascular (evidenced by lower O₂ pulse) and respiratory (lower PETCO₂) efficiencies, higher respiratory rate and VE/VO₂ at peak exercise and at AT level. However, healthy children have higher metabolic efficiency (lower R and peak VO₂, similar to those of healthy young adults).

The literature indicates possible reasons for the immaturity of the anaerobic metabolism of children during physical exercise, such as lower muscular glycogen levels, reduced activity of phosphofrutokinase-1 and of lactate dehydrogenase, and higher proportion of muscle fibers of slow contraction.

In addition, children with heart diseases usually have lower aerobic potency than young adults and children without heart diseases. Other variables derived from CPET are extremely useful to measure the response to exercise. OUES indicates systemic and pulmonary perfusion, and correlates strongly with peak VO₂. In children without heart diseases, OUES increases with their development. However, according to the study by Dias et al., in congenital heart disease, an association was identified between OUES and functional impairment severity in 59 children in the late postoperative period of congenital heart disease correction. Those authors have reported that reduced OUES was associated with low peak VO₂ (below 80% of the predicted value) in 90% of the cases, confirming the presence of a cardiovascular disorder during exertion.

In addition, ergospirometric assessment has been extremely useful in the follow-up of partially or completely treated complex congenital heart diseases, as an aid to indicate the ideal time for new therapeutic interventions. Table 1 shows the performance of children in the late postoperative period of several cyanogenic congenital heart diseases, such as Fallot tetralogy, transposition of the great arteries and single ventricle heart.
Kempny et al. have reported the reference values of the major ergospirometric variables of adults with congenital heart disease, and have correlated their data with those in the literature to guide the recreational, sports and professional activities of those individuals.

Thus, the association of cardiovascular variables, such as $O_2$ pulse and peak VO$_2$, and ventilatory variables (VE/VCO$_2$ slope) provides more comprehensive and objective data about the true functional capacity of children and adolescents with congenital heart disease. We provide major examples: after late correction of Fallot tetrotogy, evolution with pulmonary insufficiency and possible right ventricular dilation and dysfunction can indicate exchange or, currently, implantation of new prostheses, such as Melody's. CPET can indicate the best time for intervention, when the morphology of the $O_2$ pulse curve shows a depression or early plateau, in addition to ventilatory inefficiency characterized by high VE/VCO$_2$ slope values. After late correction of transposition of the great arteries according to Mustard’s or Senning’s technique, an

### Table 2 – Comparison of the ergospirometric performance of children with complex congenital heart disease and healthy ones undergoing maximal incremental test

<table>
<thead>
<tr>
<th></th>
<th>Heart disease (n = 30)</th>
<th>Normal (n = 30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>11.8 ± 6.2</td>
<td>11.9 ± 6.7</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Incremental test performance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max. velocity (km.h$^{-1}$)</td>
<td>9.8 ± 3.1</td>
<td>10.9 ± 4.9</td>
<td>0.001</td>
</tr>
<tr>
<td>AT velocity (km.h$^{-1}$)</td>
<td>5.7 ± 1.7</td>
<td>6.9 ± 1.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Max. inclination (%)</td>
<td>5.2 ± 4.8</td>
<td>6.1 ± 4.7</td>
<td>0.049</td>
</tr>
<tr>
<td>Distance (m)</td>
<td>1091.2 ± 394.1</td>
<td>1262.9 ± 307.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Time (min)</td>
<td>8.6 ± 1.5</td>
<td>11.5 ± 2.1</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting HR (bpm)</td>
<td>71.47 ± 11.3</td>
<td>79.0 ± 12.0</td>
<td>0.042</td>
</tr>
<tr>
<td>Peak HR (bpm)</td>
<td>175.9 ± 23.0</td>
<td>185.8 ± 19.7</td>
<td>0.031</td>
</tr>
<tr>
<td>Resting SBP (mmHg)</td>
<td>106.8 ± 21.4</td>
<td>106.2 ± 19.0</td>
<td>NS</td>
</tr>
<tr>
<td>Delta SBP (mmHg)</td>
<td>36.1 ± 1.1</td>
<td>39.2 ± 0.9</td>
<td>0.001</td>
</tr>
<tr>
<td>$\text{PEAK } O_2$ Pulse mL.beat$^{-1}$</td>
<td>10.4 ± 5.5</td>
<td>13.5 ± 3.6</td>
<td>0.001</td>
</tr>
<tr>
<td>$\text{AT } O_2$ Pulse mL.beat$^{-1}$</td>
<td>8.3 ± 5.1</td>
<td>12.5 ± 3.2</td>
<td>0.001</td>
</tr>
<tr>
<td>OUES</td>
<td>1693.5 ± 761.9</td>
<td>1876.6 ± 664.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>OUES/kg</td>
<td>34.1 ± 11.1</td>
<td>46.1 ± 9.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Circul. pow. (mmHg/mL/kg)</td>
<td>1924.0 ± 550</td>
<td>3937.5 ± 1220</td>
<td>0.0001</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{PEAK } VO_2$ mL.min$^{-1}$</td>
<td>1021 ± 474.2</td>
<td>1637.40 ± 634.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>$\text{PEAK } VO_2$ mL.kg.min$^{-1}$</td>
<td>31.5 ± 7.2</td>
<td>42.3 ± 7.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>$\text{VO}_2\text{AT}$ mL.min$^{-1}$</td>
<td>19.5 ± 4.5</td>
<td>25.9 ± 5.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>$\text{VO}_2\text{AT}$ mL.min$^{-1}$</td>
<td>643.4 ± 301.8</td>
<td>1004.2 ± 567.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>R ($VCO_2/VO_2$)</td>
<td>1.02 ± 0.1</td>
<td>1.04 ± 0.1</td>
<td>NS</td>
</tr>
<tr>
<td>PETCO$_2$ mmHg</td>
<td>30.83 ± 4.5</td>
<td>34.2 ± 4.0</td>
<td>0.0001</td>
</tr>
<tr>
<td><strong>Ventilatory and gas exchanges</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak VE L.min$^{-1}$</td>
<td>50.4 ± 22.0</td>
<td>55.2 ± 22.2</td>
<td>0.38</td>
</tr>
<tr>
<td>RR (rpm)</td>
<td>61.0 ± 15.2</td>
<td>58.6 ± 10.9</td>
<td>NS</td>
</tr>
<tr>
<td>PETCO$_2$ mmHg</td>
<td>32.83 ± 3.90</td>
<td>34.41 ± 3.29</td>
<td>0.0005</td>
</tr>
<tr>
<td>VE/VCO$_2$ slope</td>
<td>41.2 ± 6.40</td>
<td>35.5 ± 4.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>$O_2$ Sat (%)</td>
<td>90.9 ± 8.2</td>
<td>97.6 ± 1.2</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

AT: anaerobic threshold; HR: heart rate; peak HR: maximal HR reached; delta SBP: difference between peak and resting systolic blood pressure; OUES: oxygen uptake efficiency slope; Circul. pow.: circulatory power; $\text{PEAK } VO_2$: oxygen consumption at peak exertion; $\text{VO}_2\text{AT}$: oxygen consumption at anaerobic threshold; VE: pulmonary ventilation; RR: respiratory rate; $O_2$ Sat (%): oxyhemoglobin saturation (modified from reference 86); NS: non-significant.
older method, many children show worsening of their metabolic
efficiency (more reduced peak VO₂ and excessive ventilation –
greater VE/VCO₂ slope), which does not occur when submitted
to Jatene’s surgery, considered the ideal technique. Additionally,
CPET allows the analysis of gas exchange in other more complex
congenital heart diseases with pulmonary hypertension, such as
Eisenmenger’s syndrome. ³⁰,³¹

CPET has been a valuable complementary resource in the
follow-up of patients with congenital heart diseases to both
assess the exercise capacity and indicate the ideal time for new
therapeutic approaches, providing objective, diagnostic and
prognostic information on the patient’s true cardiopulmonary
functional status.

Author contributions
Conception and design of the research, Acquisition of
data, Analysis and interpretation of the data, Statistical
analysis, Obtaining financing, Writing of the manuscript
and Critical revision of the manuscript for intellectual
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Fernandes-Silva MM, Serra SM.

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References
1. Sociedade Brasileira de Cardiologia. [III Guidelines of Sociedade Brasileira de
2. Herdy AH, Uhnderdorf D. Reference values for cardiopulmonary exercise
European Association for Cardiovascular Prevention & Rehabilitation;
recommendations for cardiopulmonary exercise testing data assessment
Rehabilitation Prevention; Working Group on Cardiac Rehabilitation and
Exercise Physiology of the European Society of Cardiology. Statement
on cardiopulmonary exercise testing in chronic heart failure due to
left ventricular dysfunction: recommendations for performance and
interpretation. Part I: definition of cardiopulmonary exercise testing
parameters for appropriate use in chronic heart failure. Eur J Cardiovasc
5. Task Force of the Italian Working Group on Cardiac Rehabilitation and
Prevention (Gruppo Italiano di Cardiologia Riabilitativa e Prevenzione,
GICR); Working Group on Cardiac Rehabilitation and Exercise Physiology
of the European Society of Cardiology. Statement on cardiopulmonary
exercise testing in chronic heart failure due to left ventricular dysfunction:
recommendations for performance and interpretation Part III: Interpretation
of cardiopulmonary exercise testing in chronic heart failure and future
7. Almeida AE, Stefani Cde M, Nascimento JA, Almeida NM, Santos Ada C,
Ribeiro JP et al. An equation for the prediction of oxygen consumption in a
Prognostic utility of metabolic exercise testing in minimally symptomatic
patients with obstructive hypertrophic cardiomyopathy. Am J Cardiol.
Oscillatory ventilation during exercise in patients with chronic heart failure:
Review Article


