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Cardiopulmonary exercise testing in chronic obstructive pulmonary disease

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a common lung disease causing airflow obstruction and breathing problems. Despite the current advances in the treatment of COPD, exercise intolerance remains a challenge, impacting quality of life and increased morbidity. Cardiopulmonary exercise testing (CPET) is a non-invasive test with concomitant gas exchange analysis that provides a thorough assessment of exercise physiology, involving the integrative respiratory, cardiovascular, muscle and metabolic responses to exercise, and, thus providing insights into exercise limitation mechanisms. This review hypothesizes that CPET offers prognostic value in COPD and can be used to evaluate the response to several therapeutic interventions. *Aim:* To investigate the clinical usefulness of CPET in assessing exercise tolerance, disease progression and therapeutic outcomes in COPD patients. *Methods:* This this systematic literature review was conducted to analyse studies published between 2020 and 2024 on the role of CPET in COPD management. Studies were reviewed focusing on CPET's prognostic value, its correlation with disease severity, and its impact on therapeutic strategies. The quality of the selected studies was assessed by using PRISMA guidelines. *Results:* As a result, CPET-integrated monitoring supports as a valuable tool for evaluating exercise intolerance in COPD, with parameters such as peak oxygen uptake ($\dot{V}O_2$ peak), ventilatory efficiency ($\dot{V}E/\dot{V}CO_2$ slope), and dynamic hyperinflation correlating with disease severity and prognosis. According to studies a $\dot{V}O_2$ peak value below 15 mL kg^{-1} min^{-1} is associated with

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increased mortality risk and hospitalizations. Undoubtedly, CPET-derived thresholds for ventilatory and cardiovascular limitations remain an invaluable tool for COPD diagnosis and management, and contribute to optimizing rehabilitation strategies and pharmacological interventions. *Conclusion:* CPET provides important information about the pathophysiology of exercise intolerance in COPD, helping with personalized treatment planning and risk stratification. CPET should be integrated into COPD management guidelines.

KEYWORDS

chronic obstructive pulmonary disease, cardiopulmonary exercise testing, oxygen uptake, pulmonary rehabilitation

1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disease characterized by persistent airflow limitation and a chronic exaggerated inflammatory response of the airways and lungs to noxious particles or gases. Globally, COPD is one of the leading causes of morbidity and mortality with a continuously increasing prevalence and a significant impact on public health systems [1]. Given the complex nature of the pathophysiology of the disease and the limitations of resting respiratory function tests, the use of advanced and dynamic tools to assess functional capacity and guide therapeutic decisions has become necessary.

Cardiopulmonary exercise testing (CPET) is a non-invasive and integrative method used to assess the combined performance of the respiratory, cardiovascular and muscular systems during exercise. By continuously measuring gas exchange ($\dot{V}O_2$, $\dot{V}CO_2$), $\dot{V}E$, heart rate, and other physiological parameters, CPET provides detailed information on the mechanisms that limit exercise capacity in COPD patients [2, 3]. This will allow us to identify dysfunctions that cannot be observed at rest, such as ineffective ventilation, dynamic lung hyperinflation, or inadequate oxygen transport, which are common in COPD [4].

Conventional assessment of COPD severity has relied mainly on spirometry and symptomatic classification according to the guidelines developed by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). However, spirometry does not capture the complex functional limitations that occur during physical activity compared to CPET. CPET provides an analysis of the mechanisms of exercise limitation, highlighting the contribution of pulmonary, cardiovascular, and muscular deficiencies [5].

2. PHYSIOLOGY OF CARDIOPULMONARY EXERCISE TESTING IN COPD

Cardiopulmonary exercise testing (CPET) allows an integrative assessment of the physiologic response to exercise, involving the respiratory, cardiovascular and muscular systems. In patients with COPD, CPET is an essential tool to identify the mechanisms underlying exercise intolerance, based on complex pathophysiological alterations.

Physiologically, during exercise, oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) progressively increase during exercise, accompanied by an increase in pulmonary ventilation ($\dot{V}E$), heart rate and cardiac output. In COPD, these adaptations are disrupted by

ventilatory limitations, dynamic pulmonary hyperinflation, altered gas exchange, and peripheral muscle decompensation [6].

One of the most important limiting mechanisms is dynamic hyperinflation (DH), resulting from incomplete emptying of the lungs between respiratory cycles, especially during exercise. This leads to a decrease in inspiratory capacity (IC), resulting in the sensation of marked dyspnea and a reduction in the volume of air available for effective ventilation [4].

Another feature is the inefficient ventilation that is frequently observed in CPET in COPD. It is manifested by a disproportionate increase in the $\dot{V}E/\dot{V}CO_2$ ratio, which reflects the excessive ventilation required to eliminate CO_2, caused by imbalances in the ventilation/perfusion ratio and increased physiological dead space [7].

COPD patients also present with muscle damage, with reduced muscle mass and strength, especially in the lower limbs. This is manifested by an early onset of muscle fatigue and a reduced aerobic capacity, expressed by a reduction in $\dot{V}O_2$ peak [8].

On the cardiovascular side, although cardiac function is often preserved in moderate forms of COPD, a limited capacity to increase $\dot{Q}$ is often observed, particularly in patients with associated pulmonary hypertension or right ventricular impairment. In addition, exercise-induced hypoxemia and CO_2 retention may accentuate the stress on the cardiovascular system [9].

Therefore, CPET provides a detailed picture of the interplay between these systems and allows differentiation between pulmonary, cardiovascular and muscular limitations, which is essential for correct staging and personalization of therapy.

3. THE ROLE OF CPET PARAMETERS IN THE ASSESSMENT AND STAGING OF COPD SEVERITY

CPET provides important diagnostic and prognostic data, reflecting the level of functional impairment in patients with COPD. These parameters can be used both for a joint, parallel analysis of data that allows for a complete assessment of the cardiovascular, respiratory, muscular and metabolic systems during exercise. This allows us to understand the mechanisms of limitation to physical exertion, assess the severity of the disease, the risk of mortality, and the response to treatment.

3.1. $\dot{V}O_2$ peak: global marker of functional capacity

Peak oxygen consumption ($\dot{V}O_2$ peak) represents the highest level of oxygen used by the body during a progressive maximal physical effort and is considered an integrative marker of functional capacity, the gold standard in the assessment of exercise tolerance. This parameter reflects the simultaneous performance of the respiratory, cardiovascular and muscular systems.

In COPD, $\dot{V}O_2$ peak has a particular clinical value, as it allows for the global assessment of functional limitation that cannot be quantified exclusively by static tests such as spirometry. In COPD, causes leading to reduced $\dot{V}O_2$ peak include ventilatory limitation caused by airway obstruction and DH, peripheral muscle dysfunction secondary to deconditioning and systemic inflammation, as well as possible concomitant cardiac involvement [2, 9].

Numerous studies have demonstrated that peak $\dot{V}O_2$ values below 14–15 mL kg^{-1} min^{-1} are associated with an increased risk of hospitalization, reduced quality of life and higher mortality among COPD patients [10]. In contrast to FEV_1 (forced expiratory volume in one second),

which only assesses bronchial obstruction at rest and does not always correlate with symptomatology or exercise capacity, whereas $\dot{V}O_2$ peak provides a complete and objective functional picture and is considered a superior indicator for clinical staging of disease [4].

Moreover, $\dot{V}O_2$ peak is used as a reference parameter in the assessment of response to therapeutic interventions such as pulmonary rehabilitation or exercise oxygen therapy. It is also a validated predictor of survival and is frequently used as a functional endpoint in interventional clinical trials [11].

Thus, the inclusion of $\dot{V}O_2$ peak in the assessment of COPD patients provides an objective, dynamic and prognostic functional perspective, justifying the integration of CPET into algorithms for disease severity stratification and therapy personalization (Table 1).

3.2. Ventilatory efficiency and gas exchange

3.2.1. $\dot{V}E/\dot{V}CO_2$ slope. The slope of $\dot{V}E$ relative to carbon dioxide production ($\dot{V}E/\dot{V}CO_2$ slope) is a key indicator of ventilatory efficiency during exercise and reflects the ability of the respiratory system to remove CO_2 in relation to the metabolic effort expended. This parameter is derived from the linear relationship between ventilation and $\dot{V}CO_2$ up to the ventilatory threshold and is considered one of the most sensitive markers of inefficient ventilation.

The ventilatory efficiency is often expressed by the ventilatory equivalent for carbon dioxide ($\dot{V}E/\dot{V}CO_2$). This ratio, and particularly its nadir during exercise, is a sensitive marker of ventilatory inefficiency in COPD [12]. It is directly related to dead-space ventilation according to the equation: $VD/VT = 1 - 863/(PaCO_2 * \dot{V}E/\dot{V}CO_2) - VDs/VT$, where VDs represents the dead space of the measurement system. An increase in either $PaCO_2$ or $\dot{V}E/\dot{V}CO_2$ will contribute to an increased VD/VT. The $\dot{V}E/\dot{V}CO_2$ relationship is linear until the respiratory compensation point (RCP), therefore the slope is calculated in this range (approximately from 25 Watts to RCP). Reporting the slope up to peak exercise may inappropriately increase its value and is not considered standard, as it depends not only on physiological mechanisms ($PaCO_2$, $\dot{V}E/Q$ distribution) but also on how far beyond the RCP the patient can continue exercising [12].

In patients with COPD, the $\dot{V}E/\dot{V}CO_2$ slope is often increased, signaling ventilation disproportionate to the level of metabolic demand. This alteration is driven by several pathophysiologic factors characteristic of COPD, including increased physiologic dead space, ventilation/perfusion ratio imbalance (V/Q mismatch), changes in pulmonary elasticity, and abnormal ventilatory response to CO_2 [4].

Table 1. Comparison between Spirometry (FEV_1) and CPET ($\dot{V}O_2$ peak) in the assessment of functional capacity

Indicator	$\dot{V}O_2$ peak (CPET)	FEV_1 (Spirometry)
What it assesses	Global functional capacity during exercise	Severity of bronchial obstruction at rest
Type of assessment	Dynamic, integrative	Static, isolated
Relevance to exercise	High – directly correlates with exercise tolerance	Low – patients with similar FEV_1 may have different exercise tolerance
Usefulness in staging	Yes – allows functional stratification	Partial – used in GOLD classifications
Prognostic value	Very good – predictive of mortality	Limited, especially in moderate cases

$\dot{V}E/\dot{V}CO_2$ slope values >34–36 have been associated with an increased rate of exacerbations, poorer quality of life and higher mortality in COPD patients, independent of FEV1 [9]. In contrast to spirometry, which provides a static picture of obstruction at rest, the $\dot{V}E/\dot{V}CO_2$ slope allows early identification of ventilatory inefficiency in dynamics, even in patients with mild to moderate forms of COPD, in whom FEV1 may be only slightly reduced.

Furthermore, the $\dot{V}E/\dot{V}CO_2$ slope is a superior parameter for assessing the compensatory ventilatory response to exercise, providing essential information for differentiating between ventilatory and cardiovascular or metabolic limitations. In comparison, spirometry provides no information on ventilatory efficiency under physiologic stress (Table 2).

Clinical utility of CPET through $\dot{V}E/\dot{V}CO_2$ analysis:

- Allows risk stratification and assessment of severity in an objective manner;
- Helps early detection of ventilatory dysfunction in symptomatic patients with normal spirometry;
- Is a validated prognostic marker for survival and for monitoring the effectiveness of interventions (rehabilitation, oxygen therapy, bronchodilators);
- Helps guide the decision to initiate non-invasive ventilation or refer for lung transplantation [2].

Thus, evaluating patients with COPD through the $\dot{V}E/\dot{V}CO_2$ slope will provide a much more nuanced functional perspective, with superior diagnostic and prognostic value compared to traditional spirometric parameters.

3.2.2. Oxygen pulse. Oxygen pulse ($\dot{V}O_2$/HR) is defined as the ratio of oxygen uptake ($\dot{V}O_2$) divided by heart rate. This parameter indicates the oxygen consumption capacity of all body tissues per heartbeat and is determined by stroke volume and oxygen extraction by cells. The physiological relationship can be expressed as: $\dot{V}O2/HR = SV * \Delta(a\text{-}vO2)$, where SV is stroke volume and $\Delta(a\text{-}vO_2)$ is the arteriovenous oxygen difference. Although oxygen pulse is not a pure marker of cardiac performance, its behavior during CPET can provide valuable information on the integrated cardiovascular response.

In the context of COPD, oxygen pulse values are often reduced compared to the healthy population, but the exact mechanism of this phenomenon is multifactorial. Possible contributions include:

Table 2. Spirometry vs. CPET in the assessment of ventilatory efficiency

Evaluated Characteristic	Spirometry	$\dot{V}E/\dot{V}CO_2$ Slope (CPET)
Type of assessment	Static	Dynamic
Reflects ventilatory efficiency?	No	Yes – direct parameter of ventilatory efficiency
Detects V/Q mismatch?	No	Yes – indirectly through disproportionate ventilation
Prognostic value	Limited in moderate forms	High – associated with mortality and exacerbations
Sensitivity to early exercise	Low	High – detects subclinical abnormalities

- systolic volume impairment secondary to pulmonary hypertension or right ventricular dysfunction,
- chronic hypoxemia with effects on myocardial contractility,
- limitation of effort by severe dyspnea, with early cessation of the test before a maximal cardiovascular response is achieved [4, 13].

The evolution of the oxygen pulse during CPET is more important than the absolute value. In a healthy or trained patient, the oxygen pulse increases progressively during exercise, reaching a plateau only at supramaximal exercise. In contrast, in patients with COPD, one can observe:

- an early plateau of the oxygen pulse, suggesting central cardiac limitation,
- an abnormal decrease or variability, indicating hemodynamic instability or inadequate autonomic response [14].

When compared with spirometry (Table 3), oxygen pulse provides significant additional value:

- Spirometry provides no information on cardiovascular performance.
- CPET allows an integrated functional assessment of oxygen transport, revealing dysfunctions that cannot be inferred from FEV1 or flow-volume curves.

Clinical relevance:

- Oxygen pulse is a useful parameter for identifying the cardiovascular contribution to exercise intolerance in COPD.
- It is indicated in the differential diagnosis between dyspnea of respiratory and cardiac cause.
- An early plateau may guide the decision to refer for advanced cardiologic evaluation (echocardiography, catheterization, cardiac MRI).
- It is often used in combination with $\dot{V}O_2$ peak and RER to validate the patient's functional profile.

3.3. Mechanical ventilatory limitation and DH

3.3.1. Inspiratory capacity. Inspiratory capacity (IC) is the maximum volume of air that can be inspired after a normal expiration. IC remains relatively stable during exercise under physiological conditions, compared with patients with COPD in whom a progressive decrease is frequently observed. This decrease reflects the phenomenon of DH, which is, by definition,

Table 3. Spirometry vs. CPET (oxygen pulse)

Evaluated Parameter	Spirometry	CPET – oxygen pulse
Assessment of stroke volume	No	Indirect – estimated through VO_2/HR
Detects cardiovascular limitations	No	Yes – based on abnormal oxygen pulse progression
Varies with exercise?	No (static evaluation)	Yes – dynamic, progressive assessment
Usefulness in differential diagnosis	Limited	Yes – distinguishes between respiratory and cardiac dysfunction

the increase in end-expiratory lung volume (EELV) during exercise. In healthy individuals, EELV tends to decrease slightly during exercise, whereas in COPD this decrease is blunted or reversed, leading to DH. The reduction in IC is therefore the method by which DH is quantified during CPET.

During exercise, increased respiratory rate (RR) reduces the time available for expiration. In patients with COPD, this leads to incomplete emptying of the lungs and progressive accumulation of air, resulting in an increase in EELV and a corresponding measurable decrease in IC [2], which indirectly quantifies the extent of DH.

Importantly, along with the rise in EELV, the end-inspiratory lung volume (EILV) also increases, though to a lesser extent. This imbalance causes tidal volume (VT) to decrease, and in order to maintain or even increase $\dot{V}E$, the RR must rise proportionally. The higher RR shortens expiratory time, which further contributes to DH. In this context, the increased expiratory pressure promotes dynamic airway compression, explaining the appearance and progression of concavity in the expiratory flow–volume loop during exercise.

The measurement of IC during cardiopulmonary exercise testing allows direct quantification of DH. The occurrence of DH during exercise causes an increase in intrathoracic pressure, which adversely affects venous return, thereby reducing stroke volume (SV) and $\dot{Q}$. According to the literature, patients who develop DH during exercise have a significantly impaired cardiovascular response compared to those without DH. For example, the difference in $\dot{Q}$ between rest and maximal exercise ($\Delta\dot{Q}$) was significantly lower in patients with DH ($\Delta\dot{Q}$: 0.88 ± 1.35 L min^{-1}) compared to those without DH ($\Delta\dot{Q}$: 2.26 ± 1.46 L min^{-1}) [15]. A decrease in IC > 0.3 L from the resting value or a IC < 0.7 L on exertion are considered indicators of significant DH [16]. These patients often have an early cessation of exercise testing and an inability to sustain daily activities of moderate intensity. At rest, the level of hyperinflation can be directly assessed by measuring total lung capacity (TLC), EELV, and residual volume (RV) by using body plethysmography. An alternative method to assess TLC is nitrogen dilution, by determining functional residual capacity (FRC) and adding the inspiratory capacity measured at rest. However, this approach is not routinely applied in pulmonary function laboratories.

Compared to spirometry (Table 4), which only provides an indirect estimate of hyperinflation by analyzing static volumes (e.g. RV/TLC), CPET allows the assessment of these dynamics in real time, in a physiologic context. In addition, spirometry cannot reproduce the ventilatory stress conditions recorded during exercise, which limits its sensitivity in detecting functional hyperinflation.

Table 4. Spirometry vs. CPET in the assessment of hyperinflation

Evaluated Parameter	Spirometry	CPET (Inspiratory Capacity Measurement)
Detection of hyperinflation	Indirect – via RV/TLC	Direct – through measurement of IC during exercise
Dynamic assessment	No	Yes – changes observed in real time
Correlation with dyspnea	Low	High – correlates with exercise termination threshold
Sensitivity to exercise	Does not assess	High – indicates physical tolerance

Note: RV can be measured as FRC − ERV, with FRC determined either by body plethysmography or by nitrogen washout. Similarly, TLC can be calculated as TLC = FRC + IC or TLC = RV + IVC.

Clinical importance of IC in CPET:

- It is an essential parameter in identifying the mechanism of dyspnea in patients with symptoms disproportionate to spirometry;
- Provides predictive data on response to bronchodilators, oxygen therapy or rehabilitation;
- Allows differentiation between ventilatory and cardiovascular limitation;
- Is associated with reserved functional prognosis, including decreased exercise tolerance and decreased quality of life [17].

Therefore, IC is a key parameter that adds functional value to cardiopulmonary testing in COPD, providing essential information for accurate staging and guiding therapeutic decisions.

3.3.2. SEFV loop analysis and rectangular area ratio (RAR). Expiratory flow limitation (EFL) is one of the main causes of exercise intolerance in COPD. During exercise, due to increased airway resistance and reduced elastic recoil, expiration becomes partially dependent on pleural pressure, which favors dynamic airway compression. This functional change is expressed by a gradual reduction in the expiratory flow rate during the breathing cycle, emphasized by the concavity of the spontaneous expiratory flow-volume (SEFV) loop.

The extent of this concavity can be objectively quantified by the rectangular area ratio (RAR), a geometric parameter that expresses the ratio of the area under the expiratory curve to the area of a rectangle constructed from the peak expiratory flow and the forced expiratory volume. RAR values below the threshold of 0.5 are suggestive of marked concavity, significantly correlated with DH and reduced ventilatory reserve. According to a study that included 17 patients diagnosed with COPD (FEV1: 38% ± 10% of predicted value), 12 of them showed marked concavity of end-expiratory SEFV (RAR = 0.40 ± 0.03), a change that directly correlated with an increase in EELV [18].

Beyond these markedly concave curves (RAR <0.5), it is useful to recognize an intermediary group with 0.5 < RAR < ~0.7, in whom the SEFV shape already indicates airway obstruction, the presence of some degree of DH, and expiratory flow limitation; this gradation refines clinical interpretation and aligns with prior work linking concavity severity to DH during exercise [18]. Moreover, a decrease in RAR has been associated with increased airway resistance measured by impulse oscillometry, which further suggests the presence of dynamic airway compression [19].

The geometric analysis of the SEFV loop, performed during CPET, is a non-invasive, objective and reproducible method to monitor EFL and DH. Compared to classical methods such as the negative expiratory pressure (NEP) technique, which are invasive and difficult to apply under exercise conditions, this geometric approach allows continuous and real-time detection of ventilatory changes. Patients with low RAR values, specific to the heightened concavity (HCONC) group, have a more pronounced functional limitation, evidenced by increased dyspnea, reduced exercise tolerance and an increased incidence of rescue ventilation use, compared to those in the low concavity (LCONC) group [18].

Therapeutically, bronchodilation can shift patients out of the concave pattern: in GOLD 1–2 COPD with SEFV concavity, tiotropium increased end-exercise IC and raised RAR, supporting the use of RAR to track improvement in EFL/DH over time [18, 20].

Therefore, the analysis of the concavity of the SEFV loop by means of RAR complements the assessment of IC performed in the CPET, constituting an additional tool for the assessment of

the severity of DH and for a better understanding of the functional limitations encountered in COPD patients. In contrast to spirometry, which provides a static picture of lung function, CPET allows real-time, dynamic monitoring of the degree of EFL and its impact on exercise capacity [21].

3.4. Exercise intensity and metabolic response

3.4.1. Respiratory exchange ratio (RER). The respiratory exchange ratio (RER) is defined as the ratio of the $\dot{V}CO_2$ to the $\dot{V}O_2$ during exercise. This parameter reflects the metabolic balance between CO_2 production and O_2 utilization and is used to assess the degree of demand on the bioenergetic system during exercise testing (Table 5).

Physiologically, RER values increase with exercise intensification, from basal values of 0.7–0.8 (predominant fat oxidation) to ≥1.1 (maximal exercise with major glycolytic involvement and compensatory hyperventilation) [22]. Achievement of an RER ≥1.10 is commonly used as a criterion for maximal effort validity in CPET.

At the very beginning of exercise, RER may decrease transiently, because the initial CO_2 produced is buffered into body stores, so $\dot{V}CO_2$ lags behind $\dot{V}O_2$. After this early phase, RER returns to baseline resting values. At the lactate threshold, RER starts to increase, reflecting that the rate of CO_2 output rises more rapidly than O_2 uptake. This coincides with the V-slope breakpoint ($\dot{V}CO_2$ vs. $\dot{V}O_2$ slope). Importantly, this threshold should not be defined simply as RER = 1.0, but rather by the physiological inflection point where lactate buffering drives $\dot{V}CO_2$ above $\dot{V}O_2$.

At peak exercise, RER typically exceeds 1.1 and can reach even higher values. In early recovery, RER may rise further because $\dot{V}O_2$ decreases more rapidly than $\dot{V}CO_2$ clearance.

In patients with COPD, the RER may remain subunit (<1.0) during CPET for several reasons:

- Effort is interrupted early due to intense dyspnea, before reaching maximal metabolic reserves;
- DH and ineffective ventilation limit oxygen uptake and CO_2 elimination;
- here is a component of physical deconditioning or peripheral muscle damage [23].

Clinical value of RER in CPET in COPD patients:

- Confirms the level of effort reached and allows differentiation between a maximal and a subjectively limited test;

Table 5. Spirometry vs. CPET in the assessment of RER

Evaluated Parameter	Spirometry	CPET – RER
Estimates effort level achieved?	No	Yes – RER ≥1.1 indicates a valid maximal test
Reflects energy metabolism?	No	Yes – differentiates between energy substrates used
Correlation with exercise tolerance	Indirect (via FEV_1)	Yes – together with $\dot{V}O_2$ peak and test duration
Identifies early termination?	No	Yes – RER <1.0 suggests non-cardiac limitation

- Provides indirect information about the predominant mechanism of exercise limitation: a low RER associated with low peak $\dot{V}O_2$ suggests ventilatory limitation; in contrast, an RER >1.10 indicates maximal functional capacity attained;
- Is useful in monitoring rehabilitation response: trained patients tend to achieve higher RER values due to increased exercise tolerance.

Unlike spirometry, which provides a static picture and cannot validate whether the patient has reached the functional limit at rest, CPET through RER analysis allows objective assessment of the effort reached and is essential for the correct interpretation of the other parameters.

3.5. Cardiovascular adaptation to exercise

3.5.1. Chronotropic response and HR reserve. The progressive increase in heart rate during exercise is an essential component of physiological adaptation and represents a progressive increase in heart rate, which reflects the response of the autonomic nervous system and the ability of the cardiovascular system to support the increased metabolic demands of the body. In order to allow adequate cardiac output ($\dot{Q}$) and ensure efficient oxygen transport to the active muscles, ideally this increase must be proportional to the intensity of the effort.

The chronotropic reserve (the difference between the theoretical maximum heart rate and the resting heart rate) is a sensitive indicator of sympathetic autonomic function and the integrity of the cardiovascular system. In COPD, the maximal heart rate attained during exercise is often lower than that expected for age, reflecting either limitation secondary to ventilatory discomfort, autonomic dysfunction or concomitant cardiovascular pathology [14].

An insufficient chronotropic response (cardiac maladaptation to exercise) can result in a significant reduction in peak $\dot{V}O_2$ and is commonly observed in patients with moderate and severe forms of COPD. Mechanisms involved include chronic hypoxemia, systemic inflammation, direct sinus node damage, bradycardizing medication (e.g. beta-blockers) or associated autonomic neuropathy [24].

CPET allows dynamic heart rate assessment and provides indicators such as:

- heart rate attained in relation to the maximum theoretical value (HRmax),
- chronotropic reserve expressed as a percentage,
- heart rate increase curve during exercise,
- post-effort recovery time (delta HR at 1 min - autonomous prognostic marker).

Compared with spirometry (Table 6), which does not provide information about the cardiovascular response to exercise, CPET highlights the contribution of cardiac limitations to exercise intolerance. This differentiation is especially essential in symptomatic patients with relatively preserved spirometry.

Clinical relevance:

- Identification of reduced chronotropic reserve helps to differentiate between ventilatory and cardiovascular intolerance.
- A delayed post-exertional heart rate recovery (>12 bpm at 1 min) is associated with increased cardiovascular risk and higher mortality [25].
- It is a useful tool in stratifying overall risk and in deciding on referral for further cardiologic investigations.

Table 6. Spirometry vs. CPET for the assessment of cardiac response

Evaluated Aspect	Spirometry	CPET (Heart Rate and Chronotropic Reserve)
Measures cardiovascular response?	No	Yes – via HRmax, chronotropism, and post-exercise recovery
Detects autonomic dysfunction?	No	Yes – through dynamic heart rate analysis
Correlation with exercise tolerance	Indirect (via FEV_1)	Yes – directly, influences $\dot{V}O_2$ peak
Identifies extrapulmonary causes?	Limited	Yes – distinguishes cardiac from pulmonary contribution

Therefore, the analysis of chronotropic response during CPET brings considerable additional value in the multidimensional assessment of the COPD patient, allowing a more accurate functional staging and a personalized therapeutic approach.

3.5.2. $\dot{V}O_2$ recovery curve and prognostic value in COPD. Post-exercise recovery is the period during which physiological parameters return to resting values after cessation of exercise. Of these, oxygen consumption during early recovery ($\dot{V}O_2$ recovery) is an important indicator of the efficiency of the metabolic, cardiovascular and ventilatory response. Measurement of $\dot{V}O_2$ decline at 1 and 2 min post-effort can provide essential information about the body's ability to adapt and rebalance after physiological stress.

In COPD patients, $\dot{V}O_2$ recovery is frequently slowed, reflecting:

- decreased aerobic capacity,
- a persistence of DH after cessation of exercise,
- an autonomic and cardiovascular rebalancing deficit,
- impaired mitochondrial function and peripheral muscle metabolism [2, 26].

Parameters used in CPET to assess recovery include:

- $\dot{V}O_2$ delta at 1 min (the difference between maximal $\dot{V}O_2$ and $\dot{V}O_2$ at 1 min after exercise),
- duration of time for recovery of $\dot{V}O_2$ to 50% of maximum (T½ $\dot{V}O_2$),
- the complete $\dot{V}O_2$ recovery curve plotted against time.

Low delta $\dot{V}O_2$ and prolonged recovery times are associated with:

- decreased exercise tolerance,
- severe limitation of daily activities,
- inadequate response to pulmonary rehabilitation,
- unfavorable prognosis in terms of exacerbations and survival [27].

Compared to spirometry (Table 7), which does not assess any parameters in the post-exertional phase, CPET provides a dynamic and continuous picture of the patient's physiological behavior after functional stress. This is particularly important in advanced functional staging and optimization of training regimens.

Table 7. Spirometry vs. CPET ($\dot{V}O_2$ recovery curve)

Evaluated Parameter	Spirometry	CPET – $\dot{V}O_2$ Recovery Curve
Assessment of post-exercise phase	No	Yes – continuous $\dot{V}O_2$ measurement after exercise cessation
Evaluation of physiological adaptation	No	Yes – reflects efficiency of metabolic recovery
Prognostic value	Limited	High – associated with risk of hospitalization/mortality
Usefulness in rehabilitation monitoring	No	Yes – assesses response to physical interventions

Clinical utility:

- Monitoring progress in respiratory rehabilitation,
- Estimating systemic and muscular recovery capacity,
- Identification of patients with autonomic dysfunction or critical aerobic reserve,
- Integration into advanced functional assessment composite scores.

4. OVERALL PROGNOSTIC VALUE OF CPET IN COPD

Chronic obstructive pulmonary disease (COPD) is a heterogeneous condition characterized by a progressive decline in lung function and an increased morbidity and mortality rate. Although spirometry remains the standard method for diagnosis and classification, its prognostic capacity is limited, especially in terms of assessing the risk of hospitalization, mortality and response to treatment [5]. Thus, for patients with COPD, a valuable tool that allows for risk stratification and long-term prognosis is CPET, offering the possibility of an integrative and dynamic functional assessment.

Several parameters derived from CPET have been shown to have independent prognostic value:

- $\dot{V}O_2$ peak: represents the most robust predictor of survival in COPD. Regardless of the severity of spirometric obstruction, values <15 mL kg^{-1} min^{-1} obtained during CPET testing are associated with increased mortality, frequent hospitalizations, and accelerated functional decline [9].
- $VE/\dot{V}CO_2$ slope: ineffective ventilation (slope >34) is correlated with a marked imbalance between ventilation and perfusion, and has been shown to predict the risk of exacerbations, severe exercise intolerance and premature death [4].
- Markers of physiological re-equilibration capacity are the decline in $\dot{V}O_2$ during recovery and the time to return to 50% of $\dot{V}O_2$ peak. Delayed recovery in COPD patients is associated with autonomic dysfunction, fragile functional status, and poor prognosis [27].

CPET has the ability to integrate all these parameters into a complex functional profile, reflecting not only the severity of respiratory disease but also the systemic impact of the condition. In addition, CPET allows for a clear differentiation between the predominant limiting

mechanisms, facilitating the identification of high-risk patients who require more aggressive therapeutic interventions or continued surveillance.

In comparison, spirometry provides a static and partial picture, without capturing the dynamic limitations occurring under physiologic stress. Parameters such as FEV_1 and the FEV_1/FVC ratio have modest predictive utility in the absence of clinical correlation with exercise tolerance or symptomatology [5].

Thus, CPET is a complex tool with superior prognostic value compared to standard methods, justifying its widespread use not only for diagnostic and functional purposes, but also as a basis for strategic clinical decisions regarding risk assessment, therapy planning, and follow-up in COPD.

5. USING CARDIOPULMONARY EXERCISE TESTING TO PERSONALIZE PULMONARY REHABILITATION IN COPD

Pulmonary rehabilitation is an essential intervention in the management of patients with chronic obstructive pulmonary disease (COPD), with proven benefits on dyspnea, functional capacity and quality of life. However, the response to rehabilitation is often variable and depends on the individual physiologic profile. In this context, cardiopulmonary exercise testing (CPET) has emerged as a central tool for facilitating rehabilitation programs, allowing an evidence-based approach tailored to the specific mechanisms of exercise limitation [2, 28].

By integratively assessing the respiratory, cardiovascular and muscular systems, CPET provides objective information on the predominant causes of exercise intolerance. Ventilatory efficiency is best described by the $\dot{V}E/\dot{V}CO_2$ ratio and, in particular, by its nadir, which reflects the lowest point of ventilatory inefficiency during exercise and is considered the most robust index for characterizing abnormal ventilation [12]. Patients with ineffective ventilation (increased $\dot{V}E/\dot{V}CO_2$ slope and/or elevated nadir), DH (decreased inspiratory capacity), cardiovascular dysfunction (early plateau of the oxygen pulse) or peripheral muscle impairment (low peak $\dot{V}O_2$, slow recovery of $\dot{V}O_2$) can be accurately identified and fitted into distinct functional profiles [28, 9].

For example, in patients with marked DH, the integration of pursed-lip breathing techniques, the use of non-invasive ventilation during exercise, and sub-threshold training are recommended. In patients with CPET-documented cardiovascular dysfunction, workouts should be adjusted to low intensity and carefully monitored to avoid overtraining [9]. In contrast, patients with peripheral muscle damage benefit from strength exercise, nutritional supplementation and interventions tailored to low aerobic reserves [2].

Another major benefit of CPET is the possibility of establishing ventilatory thresholds (VT1 and VT2), which can be used to precisely prescribe exercise intensity. Thus, the patient is exercised in a safe, efficient and tolerable range, minimizing the risk of severe dyspnea and maximizing the physiological response to exercise [28].

In addition to personalizing the intervention, CPET has value in monitoring rehabilitation progress. Parameters such as $\dot{V}O_2$ peak, $\dot{V}E/\dot{V}CO_2$ slope and $\dot{V}O_2$ recovery can be used to assess the effectiveness of the program and to adjust the intensity or duration of sessions [2]. In addition, CPET allows the identification of non-response to rehabilitation and early reorientation of the therapeutic strategy, avoiding intervention stagnation.

In comparison, spirometry - although useful for assessing the severity of obstruction - does not provide information about dynamic functional capacity, does not allow the prescription of exercise intensity and cannot differentiate between ventilatory, cardiovascular and muscular limitations [2, 29].

Thus, CPET represents an indispensable tool for COPD patients in the respiratory rehabilitation process, providing a solid scientific basis for planning, adapting and monitoring the intervention. By integrating detailed physiological data, CPET contributes to increasing the efficiency of rehabilitation, optimizing resources and individualizing care, fundamental elements in a modern patient-centered medicine.

6. CONCLUSIONS

CPET is an essential tool in the complex evaluation of patients with COPD, going beyond the limits of conventional investigations such as spirometry. By analyzing respiratory, cardiovascular and metabolic parameters, CPET gives us a clear picture of the limiting mechanisms of effort, allowing not only the precise diagnosis of dysfunctions, but also risk stratification, prognosis assessment and personalization of therapeutic interventions.

Parameters such as peak $\dot{V}O_2$, $\dot{V}E/\dot{V}CO_2$ slope, inspiratory capacity, oxygen pulse and post-exertional $\dot{V}O_2$ dynamics provide data of high clinical value and are strongly correlated with mortality, quality of life, and response to rehabilitation. In contrast to spirometry, which exclusively assesses the severity of obstruction at rest, CPET allows dynamic characterization of the patient under conditions of functional stress, contributing to a true functional staging and a therapeutic approach focused on the individual physiological profile.

The inclusion of CPET in COPD assessment and management algorithms is justified by its ability to differentiate between ventilatory, cardiac and muscular limitations, to guide personalized respiratory rehabilitation and to anticipate evolutionary risks. Thus, CPET should not be regarded as a mere complement to functional testing, but as a central component of personalized medicine in COPD.

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