Cardiopulmonary exercise testing in patients with chronic obstructive pulmonary disease

SCOTT K. EPSTEIN, MD, AND BARTOLOME R. CELLI, MD

■ Severe chronic obstructive pulmonary disease is characterized by limited exercise capacity as a result of changes in pulmonary mechanics, abnormal gas exchange, altered cardiac function, respiratory muscle dysfunction, nutritional factors, and dyspnea. Cardiopulmonary exercise testing is a safe, effective method for objectively studying exercise performance and may be carried out using simple walk tests or more complicated treadmill or cycle-ergometry testing. Indications in patients with chronic obstructive pulmonary disease include defining the etiology of dyspnea, evaluating work disability or impairment, and assessing the response to therapy or the need for supplemental oxygen. It is also indicated in preoperative evaluation and as part of a pulmonary rehabilitation program.

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THE CAPACITY TO PERFORM exercise depends upon the ability of the cardiovascular and respiratory systems to meet the metabolic demands of the working muscles. Because exercise is constrained by the maximal rate of oxygen delivery to the exercising muscles, the cardiovascular system is the key factor that limits exercise performance[1–3] in normal individuals. However, in patients with lung disease and, rarely, in highly trained normal individuals such as marathon runners, the respiratory system may be unable to meet the physiologic demands of exercise.[4–6] In particular, patients with chronic obstructive pulmonary disease (COPD) demonstrate widely variable exercise capabilities that do not always correlate with the severity of airflow obstruction.[5,7] Cardiopulmonary exercise testing (CPET) can objectively assess the factors that result in effort intolerance.[2,3,8] Since patients with milder degrees of airflow obstruction may experience little if any reduction in exercise capacity, this review will focus on the role of CPET in patients with moderate to severe COPD.

From the Pulmonary Section, Department of Veterans Affairs Medical Center, and The Pulmonary Center, Boston University School of Medicine, Boston.

Address reprint requests to B.R.C., Chief, Pulmonary Section, Department of Veterans Affairs Medical Center, 150 South Huntington Avenue, Boston, MA 02130.

EXERCISE LIMITATION IN COPD: PATHOPHYSIOLOGIC CAUSES

Before examining the methods and indications for CPET in COPD, it is helpful to review the basis for exercise limitation in these patients.

The principal factors thought to contribute to limited exercise capacity in COPD are: 1) changes in pulmonary mechanics; 2) abnormal gas exchange; 3) respiratory muscle dysfunction; 4) altered cardiac performance; 5) nutrition; and 6) development of dyspnea. Less well-characterized factors include smoking, abnormal peripheral muscle function, and polycythemia.

Pulmonary mechanics

Patients with COPD demonstrate a limited ability to exercise, primarily because of a reduced ventilatory

capacity in the face of an increased ventilatory demand.[2,5,9,10] Because of intrinsic airway narrowing in chronic bronchitis and dynamic airway compression in emphysema, COPD is characterized by expiratory flow limitation. At rest, during tidal breathing, and universally during exercise, patients with moderate to severe obstruction frequently breathe close to or along the same flow curve as during forced (maximal) expiration.[11–13] This limitation of expiratory flow restricts the ability to meet the increased ventilatory demand of exercise.

To enhance expiratory flow and meet this demand, patients with COPD adopt two strategies. They increase inspiratory flow, reducing the time needed for inspiration, thus allowing more time for expiration.[14,15] They also increase end-expiratory lung volume, reducing the effects of intrinsic airway narrowing and dynamic airway compression.[14–17] Both of these mechanisms should result in increased ventilation. Unfortunately, the former strategy increases the resistive work of breathing (increased flow leads to increased resistance), while the latter increases inspiratory elastic work (see below).[17] Any increment in the work of breathing impairs respiratory muscle efficiency and leads to fatigue, further reducing ventilatory capacity.

The ventilatory demand of exercise in COPD greatly exceeds that in normal patients for a similar work load.[2,8,18] For any given task, a greater level of ventilation is required and, thus, maximal ventilatory capacity is reached sooner. At rest, COPD is characterized by marked ventilation-perfusion mismatch that results in increased dead-space ventilation (dead space/tidal volume—ie, areas that are ventilated but hypoperfused) and increased pulmonary shunt (areas hypoventilated but normally perfused).[18] The increase in dead-space ventilation means greater wasted ventilation and, thus, a higher minute ventilation for a given work load.[19,20] In COPD, unlike normal pulmonary conditions, dead-space ventilation often does not fall with exercise, leading to a markedly increased ventilatory demand for any given work load.[2,18] Increases in pulmonary shunt fraction, which may be magnified during exercise, result in hypoxemia with subsequent carotid chemoreceptor stimulation and a further increase in the ventilatory requirement.

Gas exchange

In normal patients and in some patients with COPD, progressive exercise is characterized by anaerobic metabolism as aerobic capacity is exceeded. Rising lactate production is initially buffered by bicarbonate, resulting in increased production of carbon dioxide. Later, the bicarbonate concentration falls and pH decreases. These events provide a powerful stimulus for increased ventilation in order to prevent partial pressure of carbon dioxide (PCO_2) from rising and to check metabolic acidosis. Consequently, at peak exercise (after the anaerobic threshold has been crossed), normal patients will manifest a respiratory alkalosis and only a modest decrease in blood pH. In COPD, because of the mechanical abnormalities noted above, ventilation may not increase appropriately, resulting in uncompensated metabolic acidosis.[2] In some patients PCO_2 may rise, leading to respiratory acidosis with an adverse effect on respiratory muscle function.[21–23]

Hypoxemia may be present at rest or may occur during exercise. It can limit exercise capacity through a host of mechanisms: (1) carotid body stimulation with increased ventilation for a given work load[18,24,25]; (2) increased pulmonary artery resistance secondary to hypoxic vasoconstriction, leading to elevated right ventricular afterload and reduced cardiac output[26–28]; (3) decreased oxygen delivery to cardiac and peripheral skeletal muscle[24,29]; (4) decreased oxygen delivery to respiratory muscles, increasing the susceptibility of these muscles to fatigue[30]; (5) achievement of an early anaerobic threshold, causing an increase in ventilatory load[31,32]; and (6) increased sense of dyspnea.

Respiratory muscle dysfunction

Patients with COPD often have impaired respiratory muscle function at rest.[33,34] Our group[35] studied 67 patients with COPD and found that maximal transdiaphragmatic pressure was reduced. Decreased maximal transdiaphragmatic pressure correlated best with forced expiratory volume in 1 second (FEV_1, a measure of obstruction), functional reserve capacity/total lung capacity (hyperinflation), and albumin (nutrition).[35] When the ratio of transdiaphragmatic pressure (tidal breath) to maximal transdiaphragmatic pressure is greater than 40%, respiratory muscle fatigue will occur.[36] Inspiratory muscle fatigue may limit exercise capacity, because at rest, and certainly during exercise, patients with COPD breathe close to this fatigue threshold.[30,36–38]

As noted earlier, exercise in COPD is associated with dynamic hyperinflation, which adversely affects respiratory muscle function through several mechanisms. It increases the load on the inspiratory muscles because breathing now takes place on the non-

compliant region of the lung's pressure-volume curve. The flattened diaphragm is a less effective pressure generator because of a decreased zone of apposition, a horizontal rather than vertical orientation of muscle fibers, and an increased radius of curvature. It results in a positive airway pressure at end-exhalation as the system is still recoiling inward when the next breath is taken.[39,40] This intrinsic positive end-expiratory pressure (or auto-PEEP) constitutes an inspiratory load that must be overcome before gas will flow into the lungs.[39,40] O'Donnell et al[39] and Petrof et al[40] have confirmed the importance of this by using continuous positive airway pressure to overcome this inspiratory load, decrease the work of breathing, and improve exercise endurance in COPD.

In normal patients, the respiratory muscles use only 1% to 2% of oxygen uptake at rest; with exercise this increases to 10% to 15%.[41] The oxygen cost of breathing is considerably higher in COPD, reaching values of 35% to 40% during exercise.[41] This high oxygen consumption by the respiratory muscles limits the supply of oxygen to the heart and the peripheral muscles.

The high oxygen consumption by the ventilatory muscles is due not only to increased minute ventilation, but also to the recruitment of the accessory muscles of respiration.[38,42–46] Our group has shown that as the severity of COPD increases there is a shift in the way that respiratory muscles are recruited: the rib cage accessory and abdominal muscles, rather than the diaphragm, become the principal pressure generators.[42] Many of these muscles participate in both ventilatory and nonventilatory activity and their uncoordinated recruitment may result in disproportionate use of oxygen, which further decreases oxygen supply to other tissues.[43–45]

Cardiac dysfunction

Although exercise in most patients with COPD is limited by ventilatory factors, there is now substantial evidence that exercise-associated cardiac dysfunction is common in these patients. Right ventricular abnormalities are frequent at rest, even in the absence of cor pulmonale, and this may limit exercise performance in COPD.[26,27,47,48] Right ventricular dysfunction occurs in 40% of patients with $FEV_1 < 1.0$ L and in 70% with $FEV_1 < 0.6$ L.[47]

In normal patients, exercise is accompanied by recruitment of small pulmonary arterioles and capillaries that allow cardiac output to increase without significantly altering pulmonary vascular resistance or pulmonary artery pressure. In COPD, the pulmonary vascular bed may not be "recruitable" because of hypoxic vasoconstriction, secondary remodelling of vessels, and parenchymal lung destruction, with reduction of vascular cross-sectional area.[47] Thus, in COPD, exercise is frequently associated with an increase in pulmonary vascular resistance and pulmonary artery pressure.[26–28,47] Because of the resulting increase in right ventricular afterload, right ventricular ejection fraction does not rise appropriately in more than 70% of exercising COPD patients.[26]

Whether left ventricular systolic dysfunction is associated with COPD is controversial. Left ventricular hypertrophy or reduced left ventricular ejection fraction have been demonstrated in 24% to 86% of patients with COPD; however, these abnormalities could have resulted from concomitant hypertension or coronary artery disease.[26,49–52]

On the other hand, there is evidence for left ventricular diastolic dysfunction associated with COPD. Left ventricular filling decreases as pulmonary vascular disease and right ventricular dysfunction reduce the volume of blood flowing from right ventricle to left ventricle (reduced left ventricular preload). In addition, as the right ventricle becomes overloaded, the interventricular septum shifts, altering the geometry of the left ventricle and further restricting left ventricular filling.[26,50,53]

Nutrition

Nutritional abnormalities are common in COPD and may impair exercise capacity by reducing respiratory and peripheral muscle function.[54–58] In addition, COPD patients who are fed a carbohydrate load have reduced exercise capability[59]: the excess carbohydrate results in increased production of carbon dioxide, necessitating an increased minute ventilation for any given work load. Nevertheless, the true importance of nutritional factors in the exercise limitation of patients with COPD remains controversial.

Dyspnea

The pathogenesis of the perception of shortness of breath is very controversial. In addition to occurring as a consequence of the factors mentioned above, dyspnea may also relate to an abnormal sensation of respiratory loads.[60,61] This concept is supported by studies showing reduced dyspnea and increased exercise tolerance after treatment with dihydrocodeine, promethazine, and ethanol.[62] Dyspnea is important because of its frequency; however, a detailed discussion of the genesis and evaluation of dyspnea is beyond the

TABLE 1
CORRELATION OF LEVELS AND VARIABLES IN CARDIOPULMONARY TESTING

Levels	Variable	Method of measurement
1*, 2†, 3	Exercise capacity	Distance walked (level 1) or Watts achieved (levels 2 and 3)
	Heart rate	Physical exam (level 1) or continuous electrocardiogram (levels 2 and 3)
	Respiratory rate	Physical exam (level 1) or metabolic cart (levels 2 and 3)
	Blood pressure	Cuff
	Dyspnea	Borg or visual analogue scale
2, 3	Tidal volume	Timed gas collection or metabolic cart
	Minute ventilation	"
	Oxygen uptake	"
	Carbon dioxide production	"
	Respiratory quotient	"
	Anaerobic threshold	"
	Oxygen saturation	Oximeter (ear or finger)
3	pH	Arterial blood gas
	Partial pressure of carbon dioxide	"
	Partial pressure of oxygen	"
	Dead space/tidal volume	"
	Alveolar-arterial oxygen gradient	"
	Pulmonary arterial pressure	Swan-Ganz catheter
	Pulmonary vascular resistance	"
	Cardiac output	"

*Eg, 6-minute or 12-minute walk test
†Eg, treadmill or cycle test

scope of this article. Several recent publications address these topics in detail.[63–65]

Smoking

Chronic cigarette smoking reduces exercise endurance, but the role of concomitant lung disease may be difficult to determine, given the close association of the two.[66] In normal patients, acute smoking reduces tissue-oxygen delivery (through the action of carbon monoxide and nicotine), increases cardiac work, and increases dead space.[66] It would not be surprising if similar effects occur in patients with COPD.

Peripheral muscles

Many patients, with or without COPD, stop exercising because of "leg fatigue." Abnormal limb fatigue may contribute to exercise limitation in COPD.[67] The protein calorie malnutrition seen with COPD affects peripheral skeletal muscles as well as respiratory muscles. Weakness and atrophy of limb muscle may result in reduced motor efficiency and limited aerobic capacity.[56,57,68] In turn, this may increase the oxygen requirement for these exercising muscles or precipitate a premature sense of leg discomfort or fatigue.[2] Either of these conditions would result in early termination of exercise.

Polycythemia

Chronic or intermittent hypoxemia may lead to polycythemia, which can adversely effect right ventricular function. In polycythemia, increased serum viscosity increases right ventricular afterload, and increased intravascular volume increases right ventricular preload.[47] Phlebotomy in hypoxemic COPD patients improves right ventricular ejection fraction and exercise endurance.[47]

EXERCISE TESTING METHODS

The elements of the various levels of exercise testing are detailed in *Table 1*. The 6-minute and 12-minute walk tests correlate both with static pulmonary function and with maximal oxygen uptake and ventilation, but they are not taxing enough for most patients with less severe COPD.[69,70] "Stair climbing" is more demanding but has never been standardized as a test. Pollock et al[71] performed a stair-climbing test on 35 patients with different degrees of airflow obstruction. The number of stairs (or steps) climbed correlated significantly with peak oxygen uptake and minute ventilation. If confirmed, stair climbing may provide an important tool for simple testing of patients with less severe airflow obstruction.

The response to a given intensity of exercise (expressed by physical work performed) can be determined and the factors contributing to exercise limitation can be distinguished with the additional analysis of expired gas. The gas is collected over time in special impermeable bags and then sampled for oxygen and carbon dioxide concentration. More recently, metabolic "carts" that analyze the composition of expired gas have simplified this task. The patient breathes through a low-resistance mouthpiece with a nose clip in place. A

pneumotachygraph measures tidal volume, respiratory rate, and minute ventilation from the flow signal. Expired gas is continuously sampled to measure oxygen uptake and carbon dioxide production. Blood gases are obtained from an indwelling brachial artery catheter or from discrete radial artery punctures (once prior to onset of exercise and once at peak exercise). Surface electrocardiogram electrodes allow for continuous monitoring of heart rate and rhythm; in addition, the 12-lead electrocardiograph is monitored prior to exercise, every 2 minutes during exercise, and during the recovery period. Blood pressure is obtained via the arterial catheter or by repeated measures using a cuff. Ear or finger oximetry is used to assess changes in oxygen saturation.

$$(1)\ \text{Cardiac output} = \text{Stroke volume} \times \text{heart rate} = \frac{\text{Oxygen uptake}}{\text{Hemoglobin } (Sa_{O_2} - Sv_{O_2})}$$

$$(2)\ \text{Oxygen pulse} = \frac{\text{Oxygen uptake}}{\text{Heart rate}} = \text{Stroke volume} \times \text{hemoglobin } (Sa_{O_2} - Sv_{O_2})$$

FIGURE. Fick equation (1) rearranged to derive oxygen pulse (2). Sa_{O_2}, arterial blood oxygen saturation; Sv_{O_2} mixed venous blood oxygen saturation.

Exercise testing can be performed using either a treadmill or an electronically braked cycle ergometer. We prefer cycle ergometry because it allows more accurate determination of work performed[72]: in contrast, work performed on a treadmill is influenced by body weight, length of stride, and the mechanical efficiency of walking technique.[19,72,73] Exercise protocols may include submaximal or maximal tests and may employ either a continuously or incrementally rising work load. We prefer a "symptom-limited" (maximal) test in which a short period of pedalling with no work load is followed by an incrementally increasing work load. At submaximal exercise, cycle ergometry and treadmill yield similar values for oxygen uptake, heart rate, and minute ventilation, though there may be wide variation in some patients.[74] At maximal exercise the cycle generally results in lower maximal oxygen uptake.[75] Unfortunately, cycle ergometry may underestimate exercise-related oxygen desaturation.[76]

Interpretation of exercise tests in COPD

Exercise testing generates metabolic, cardiovascular, and ventilatory measurements. These can be compared with predicted values in normal patients and related to one another in order to generate defined patterns of normality and abnormality.[2,3,8] Patients with more severe COPD often show a characteristic pattern of abnormality. Patients with mild disease often have no ventilatory limitations and may perform normally during CPET, or they may demonstrate abnormalities consistent with cardiac disease or deconditioning that may have been concealed by respiratory constraints.

The predicted maximal heart rate (in beats per minute) for a given patient is calculated by subtracting the patient's age (in years) from 220. At peak exercise, normal patients, deconditioned patients, and patients with cardiac disease will have little if any heart rate reserve (ie, will have achieved greater than 85% of predicted maximal heart rate). Patients with COPD usually have a large heart rate reserve (> 20%), since cardiovascular limitations on exercise are not achieved.

Although many formulas (principally using the FEV_1) can estimate maximal ventilatory capacity, we prefer using the results of a 12-second maximal voluntary ventilation test, or alternatively, $FEV_1 \times 40$.[2,4,8] Normal patients, deconditioned patients, and cardiac patients have abundant ventilatory reserve at peak exercise (maximal voluntary ventilation – maximal minute ventilation > 20 L).[2] In contrast, ventilatory limitation is characteristic of COPD, with the breathing reserve often approaching zero.[2]

Oxygen uptake at peak exercise (maximal oxygen uptake) is usually reduced in COPD.[74,77] In cardiac disease or deconditioning, similar decreases result from inadequate oxygen delivery to, or utilization by, the exercising muscles; in COPD it usually results from exercise terminating at a lower work load because of ventilatory limitation. Because oxygen delivery and utilization are often normal, anaerobic metabolism (as measured by the anaerobic threshold) may occur only late or not at all.[24,31,32] When disease is less severe, the anaerobic threshold is frequently achieved.[78]

Oxygen pulse (oxygen uptake divided by heart rate) is frequently assessed during CPET; its usefulness in estimating stroke volume can best be understood by rearranging the Fick equation (*Figure*). In normal patients, oxygen pulse increases during exercise, principally because of a widening difference between

TABLE 2
USES OF CARDIOPULMONARY TESTING IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Defining the etiology of dyspnea
Assessing disability
Evaluating for thoracotomy
Assessing response to therapy
Assessing need for supplemental oxygen
Evaluating for pulmonary rehabilitation
Research protocols

arterial and mixed venous oxygen concentrations. If cardiac disease is present (ie, stroke volume is reduced), the oxygen pulse may be low at peak exercise. Oxygen pulse is also low in COPD; however, this is likely not a result of reduced stroke volume, because when the oxygen pulse is plotted against the work load, the rate of rise (slope of the curve) is normal.[21] Rather, the absolute value is low because exercise is terminated early (at a low work load) due to ventilatory limitation.

Exercise-induced changes in blood gases are common in COPD. At rest, hypoxemia (with a widened alveolar-arterial oxygen gradient) often occurs as a result of ventilation-perfusion mismatching. Arterial partial pressure of oxygen (and oxygen saturation) may fall with exercise, especially when the diffusing capacity for carbon monoxide is low.[79] But in contrast to changes seen in pulmonary fibrosis or pulmonary vascular disease, there is typically no further widening of the alveolar-arterial oxygen gradient.[2] The ventilation-perfusion mismatch of COPD may also result in an increase in the difference between arterial P_{CO_2} and end-tidal P_{CO_2}; this difference does not decrease with exercise, as is the case in normal patients.[2] Because of this highly inefficient pattern of ventilation, patients with COPD may not develop adequate respiratory compensation for the metabolic acidosis associated with the anaerobic threshold.[2]

INDICATIONS FOR EXERCISE TESTING

For patients with COPD, exercise testing provides an objective measure of exercise capacity in a number of conditions and situations (*Table 2*). Exercise testing is exceedingly safe, with a reported mortality of less than 0.01%, and clinicians who do not have access to a sophisticated CPET laboratory may still perform CPET using relatively simple techniques.[8]

Dyspnea

Dyspnea is an extremely nonspecific symptom: it may be a manifestation of lung or cardiac disease, anemia, deconditioning, or psychological problems. Within the category of lung diseases, dyspnea may result from airway obstruction (COPD, asthma, upper airway obstruction), interstitial disease, pulmonary vascular problems, or pleural, chest wall, and respiratory muscle disease. Even if the patient unequivocally has COPD, the degree of dyspnea may seem out of proportion to the degree of spirometric abnormality.

Since dyspnea is most commonly present only during exertion, causative factors may only become apparent during exercise. Exercise may be limited by nonventilatory factors in 25% to 30% of patients with COPD, and in this group treatment aimed solely at COPD may be inappropriate or inadequate.[6,80] Perhaps the most common dilemma is deciding whether dyspnea is a result of COPD, cardiac disease, or both. The incidence of COPD and coronary artery disease increases with age and is closely tied to tobacco use; hence, the diseases frequently coexist. To further confuse matters, the usual clinical findings of left ventricular failure may be found in COPD alone.[81] CPET is effective in defining the relative contributions of cardiac and lung disease to dyspnea.[2,3,8,21,72] Not uncommonly, in our experience, effective treatment for COPD may uncover significant symptomatic cardiac disease.

Assessment of disability

Exercise testing is an important tool in the evaluation of disability. It provides an objective and quantifiable measure of exercise impairment and can implicate or exonerate the lungs as the culprit. In a study of 348 retired shipyard workers with possible exercise limitation, Oren et al[80] found a poor correlation between standard pulmonary function tests and work capacity; they also found that cardiovascular rather than respiratory disease was the more frequent cause of impairment.[80]

The American Thoracic Society has defined severe impairment as either $FEV_1 < 40\%$ of predicted value or forced vital capacity (FVC) < 50% of predicted value (step I), or a diffusing capacity for carbon monoxide < 40% of predicted value (step II).[82] Unfortunately, in COPD these values may not be sufficiently sensitive or specific to identify respiratory impairment.[82,83] Furthermore, the working capacity of patients with ventilatory limitation is difficult to predict without direct measurement.

Assessment of capacity to work via direct measure-

ment of maximal oxygen uptake (step III) is recommended when step I or II values indicate severe impairment and the individual claims to be "unable to do the physical demands of the job secondary to shortness of breath," or when steps I and II are inadequate.[82] For step III, impairment is considered severe when 30% to 40% of the maximal oxygen uptake is insufficient to meet the oxygen uptake of a specific job activity or when the maximal oxygen uptake is less than 15 mL/kg/minute.[82] Estimated values for the oxygen uptake associated with various activities and occupations are readily available.[2]

Preoperative evaluation

Patients undergoing pulmonary resection for lung cancer have a postoperative mortality of 4% to 10% and a morbidity of 10% to 70%.[84,85] Static pulmonary function tests have been used to predict the risk of post-thoracotomy complications. Patients with severe impairment of ventilatory function are considered at high risk for postoperative difficulties.[86–88] However, some of these "high-risk" patients experience no postoperative complications, whereas other "low-risk" patients with only mild or moderately abnormal pulmonary function may develop serious postoperative complications. Thus, static pulmonary function criteria are neither sensitive nor specific predictors of the postoperative course.[84,85]

Several recent studies have used CPET to better define patients at increased risk. Results from these studies suggest that a maximal oxygen uptake > 20 mL/kg/minute is associated with minimal risk, whereas a maximal oxygen uptake < 10 to 15 mL/kg/minute portends an adverse outcome.[84,85] Unfortunately, other studies have not shown that maximal oxygen uptake predicts post-thoracotomy morbidity and mortality.[89,90] Interestingly, none of these studies examined other methods of risk stratification.

We retrospectively reviewed the course of 42 patients who had CPET prior to lung cancer resection.[91] We used a cardiopulmonary risk index combining cardiac evaluation (modeled on the Goldman criteria) and pulmonary evaluation for the following risk factors: obesity, tobacco use within 8 weeks of surgery, $FEV_1/FVC < 70\%$, $P_{CO_2} > 45$ mm Hg, and productive cough or diffuse wheezing within 1 week of surgery.[92] One third of the patients suffered at least one postoperative complication. When we stratified patients according to maximal oxygen uptake per body surface area, complications and a cardiopulmonary risk index ≥ 4 were found to be more common in patients whose oxygen uptake per body surface was < 500 mL/m^2/minute: the incidence of complications was 64% vs 23% ($P < .05$), and a high risk index was seen in 73% vs 23% ($P < .005$). Adding maximal oxygen uptake to the cardiopulmonary risk index did not improve the ability to predict postoperative complications. Thus, the role of preoperative CPET remains controversial. We are currently examining this issue in prospective fashion.

Response to therapy

Response to therapy for COPD (bronchodilators, steroids) is usually evaluated in terms of improvement in spirometric measurements or subjective improvement in symptoms. Since a goal of therapy for COPD is to decrease dyspnea, which most commonly occurs with exertion, CPET should be an ideal tool to objectively assess the efficacy of treatment. However, surprisingly few studies have examined this issue, and the results of these reports have been mixed.[4,93,94] CPET can effectively quantify the response to supplemental oxygen and can monitor the response to treatment for congestive heart failure.[25,30,95]

Pulmonary rehabilitation

Although pulmonary rehabilitation has not been shown to improve survival in COPD, it often results in symptomatic improvement and increased exercise endurance.[96] CPET may serve several functions within a pulmonary rehabilitation program.

Referral for pulmonary rehabilitation nearly always results from complaints of severe, often disabling dyspnea, despite maximal therapy for COPD. As noted earlier, up to one third of such patients may be limited by nonventilatory factors. In these patients, CPET may help define the cause of dyspnea.

CPET may also predict the likelihood of response to pulmonary rehabilitation. Casaburi et al[97] have argued that only patients who develop elevated blood lactate (metabolic acidosis) with exercise will respond to exercise training. The excess lactate produced at the anaerobic threshold is initially buffered (resulting in increased CO_2 production) and then, later, causes pH to fall. These changes provide a powerful stimulus for increased ventilation, thus limiting exercise at a lower work load. With exercise training, aerobic capacity improves, delaying the onset of anaerobic metabolism. Maximal ventilation is then reached at higher work loads, and exercise capacity improves.

Recently, Casaburi et al have shown that most patients with mild-to-moderate COPD (mean FEV_1

1.70 to 1.87) increase blood lactate at low work rates.[78] Furthermore, they showed that a physiologic training effect was better achieved with training at high rather than low work rates. Thus, in some patients, CPET may be able to predict the likelihood of response to training. Patients with more severe COPD are less likely to achieve the anaerobic threshold during CPET and may not benefit from exercise training.[24,31,32]

It could then be argued that patients with ventilatory limitation (ie, do not achieve anaerobic threshold) should be excluded from exercise training. Our group has shown that pulmonary rehabilitation consisting solely of unsupported arm training improves endurance for unsupported arm exercise; the metabolic and ventilatory costs of exercise improve as well.[98] This type of exercise is not characterized by anaerobic metabolism at peak exercise. We have concluded that metabolic and ventilatory improvements likely result in part from enhanced muscular coordination, strength, and efficiency. Similar responses may occur in other skeletal muscle groups after more traditional exercise training.

CPET has been used by several groups to individualize the intensity of the training program; moreover, CPET provides an easy objective measure of improvement in exercise capacity after completion of pulmonary rehabilitation.[99,100] The response to exercise has been used to evaluate other system functions (cardiovascular, hematologic, neurologic) and as an endpoint for multiple interventions. As such, exercise testing has become an often-used research tool. As we standardize its application, it can become a useful tool to compare results from different laboratories.

SUMMARY

Patients with COPD manifest an array of physiologic respiratory abnormalities that lead to a reduced capacity for exercise. CPET is a safe and effective method for quantifying and defining the nature of this limitation. It is a useful clinical tool for determining the cause and severity of dyspnea and the presence of disability or impairment. It can serve several important roles in a program of pulmonary rehabilitation. The role of CPET in the preoperative evaluation of patients awaiting thoracotomy for lung cancer resection remains controversial.

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