Use of the Breathing Reserve To Interpret Submaximal Exercise Responses

Interpretation of cardiorespiratory exercise tests (CPEX) typically is based on measurement of peak exercise responses compared with predicted maximal values in order to estimate the reserve capacities of the cardiovascular and respiratory systems. However, this may be a problem if the patient does not want or is unable to tolerate whatever subjective discomfort occurs and stops exercising before achieving the expected cardiac (at least 85% of predicted maximal heart rate) or respiratory (at least 70% of predicted maximal ventilation) response. Although a patient with a musculoskeletal disorder also may not achieve these exercise “targets,” in most cases the CPEX is interpreted as “submaximal responses or poor effort.”

In this issue of CHEST, Medoff and colleagues (see page 913) examined the breathing reserve (peak exercise ventilation/maximal voluntary ventilation [MVV]), an established method for interpreting CPEX, at an identifiable submaximal intensity, the lactate threshold. These investigators hypothesized that the breathing reserve measured at the lactate threshold would be useful to indicate a pulmonary limitation (PML) to exercise. Over a 4-year period, they identified 12 persons who exhibited normal cardiorespiratory responses, 32 patients with COPD who had PMLs to exercise, and 29 patients with known or suspected cardiac disease who had cardiovascular limitations to exercise. Of note, 21 other patients with COPD were excluded from the analysis because a lactate threshold was not evident during CPEX.

The major findings of the study were that the breathing reserve at the lactate threshold and at peak exercise were highly correlated (r = 0.85) and that the breathing reserve at the lactate threshold was significantly higher for the patients with PML than for those in the cardiovascular limitation or normal groups. In fact, a value of 0.42 or higher for the breathing reserve at the lactate threshold predicted a PML with a sensitivity of 97% and a specificity of 95%.

A few questions are appropriate in consideration of these findings. First, does an abnormal breathing reserve reflect a PML to exercise? As pointed out by Medoff and colleagues, other pathophysiologic mechanisms may limit exercise in COPD. Such mechanisms include hypoxemia, dynamic hyperinflation, and/or respiratory muscle dysfunction as major possibilities. Until additional methods have been evaluated (eg, flow volume loops during exercise), the use of the breathing reserve remains an established approach for interpretation purposes. Second, how should the MVV be determined? The two usual choices are to measure ventilation over 12 s or to calculate the value based on the FEV₁ Medoff and colleagues chose to calculate the MVV by multiplying the FEV₁ by 40. In our laboratory, each patient performs the MVV maneuver twice (with a rest between efforts) before the exercise test. The highest value among the two MVV efforts and FEV₁ multiplied by 40 is then selected. Usually, but not always, the values are close. Third, can noninvasive methods be used to estimate the lactate threshold? Although the investigators in this study collected serial samples of arterial blood to determine the lactate threshold, this approach is not practical for the majority of clinical CPEX. Furthermore, such measurements add considerably to the cost of exercise testing. Therefore, the V-slope method (the point at which carbon dioxide production begins to increase more rapidly than oxygen consumption) is being used in many laboratories to identify (estimate) the onset of metabolic acidosis during exercise. Finally, are the results applicable to patients with other respiratory conditions such as interstitial lung disease or pulmonary vascular disease? The answer to this question presently is unknown, and additional studies are required.

Despite these uncertainties, the results of this study provide new information to advance the un-

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Understanding of the interpretation of CPEX in patients who have reduced effort or perform submaximal exertion. The investigation by Medoff and colleagues is an excellent example of clinical research with direct application to patient care. Like all initial findings, prospective testing should be performed to validate the approach and to examine results in patients with other respiratory disorders.

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It’s Not “Just a Virus” Anymore

When I attended medical school 20 years ago, there was essentially no discussion of viruses on the medical wards. Knowledge of viruses was historical (influenza epidemics, including the pandemic in 1918-19), esoteric (eg, equine encephalitis), or of little clinical importance because most viral infections were self-limiting and no therapy was available.

The clinical importance of viral infections changed dramatically over the next decade with dissemination of the HIV virus, the cause of AIDS. In addition, the number of solid organ and bone marrow transplantations increased rapidly, and it quickly became appreciated that cytomegalovirus (CMV) infections were causing significant morbidity and mortality in transplant recipients.

Nevertheless, most of the “ubiquitous viruses” that commonly cause self-limiting viral syndromes in children and adults received rather little attention. However, information gathered over the last several years suggests that these viruses are significant pathogens in transplant recipients. Including lung transplant patients.2,3 A recent animal study4 suggested that lung transplant recipients may be partially susceptible to viral respiratory infections because of an inadequate antibody response.

In this issue of CHEST (see page 944), Palmer and associates have further extended our knowledge of these viral infections in lung transplant recipients. In their retrospective review, 10 of 122 (8%) of their adult lung transplant recipients developed non-CMV respiratory viral infection. Adenovirus, respiratory syncytial virus, and parainfluenza 3 were the pathogens identified in the 10 patients. All 10 had symptoms of respiratory infection; 3 developed acute respiratory failure that required mechanical ventilation, and 2 died.

The authors identified intriguing data that four of eight lung transplant recipients who survived non-CMV viral pneumonia developed obliterator bronchiolitis (OB), which was higher than the 20 to 25% incidence of OB in their transplant center. The postulation on the basis of these data that viral infection can cause or exacerbate OB is suspect given the small number of patients in their retrospective study. Nevertheless, there is pathophysiological evidence to support this theory. Winter and colleagues5 demonstrated that rats that received allogenic lung transplants infected with parainfluenza 1 developed OB, whereas rats that received uninfected transplants had practically normal airways. In addition, some viral infections can cause OB-like lesions.6

Although the association of viral infection with OB is based on a paucity of data, it should be pursued because OB is the single most important limitation to medium-term and long-term survival after lung transplantation, and presently there is no effective therapy for OB.7 Perhaps viruses are “the missing link” to the cause of OB, and maybe antiviral therapy, vaccination, and viral avoidance will be more effective in lowering the incidence of OB than the development of new immunosuppressive drugs.

Even if there is no virus-OB connection, the clear message of the study by Palmer and colleagues is that non-CMV viruses must be considered as a cause of pulmonary infection after lung transplantation and may lead to respiratory failure and death. These pathogens should be searched for in lung transplant recipients with respiratory symptoms. Because these infections are potentially life-threatening, antiviral therapy should be considered for certain pathogens, even if evidence for their use is controversial (eg, ribavirin for respiratory syncytial virus). Lung transplant recipients must be vigilant to avoid possible sources of viral infection, such as close contact with family, friends, and children with respiratory symptoms. Clearly, we cannot say “it’s just a virus” anymore.

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