

2

Cardiopulmonary Exercise Testing in the Evaluation of the Patient with Emphysema

*David Balfe, MBBCH, FCP (SA)
and Zab Mohsenifar, MD, FCCP*

CONTENTS

INTRODUCTION
BROAD OVERVIEW OF METHODS OF CARDIOPULMONARY EXERCISE TESTING
SAFETY ISSUES IN CARDIOPULMONARY EXERCISE TESTING
SPECIFIC ISSUES RELATING TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND EMPHYSEMA
TYPES OF CARDIOPULMONARY EXERCISE TESTING FOR PATIENTS WITH COPD
RESPONSES TO EXERCISE IN CHRONIC OBSTRUCTIVE LUNG DISEASE
DYNAMIC HYPERINFLATION AND ITS CONSEQUENCES
CARDIOVASCULAR RESPONSE TO EXERCISE IN COPD PATIENTS
EFFICACY OF LVRS
REFERENCES

INTRODUCTION

Comprehensive exercise testing offers an opportunity to study the cellular, cardiovascular, and ventilatory systems' responses simultaneously under controlled conditions (1). Physical exercise requires the interaction of physiologic mechanisms that enable the cardiovascular and respiratory systems to supply exercising muscles with the fuel

From: *Lung Volume Reduction Surgery*

Edited by: M. Argenziano and M. E. Ginsburg © Humana Press Inc., Totowa, NJ

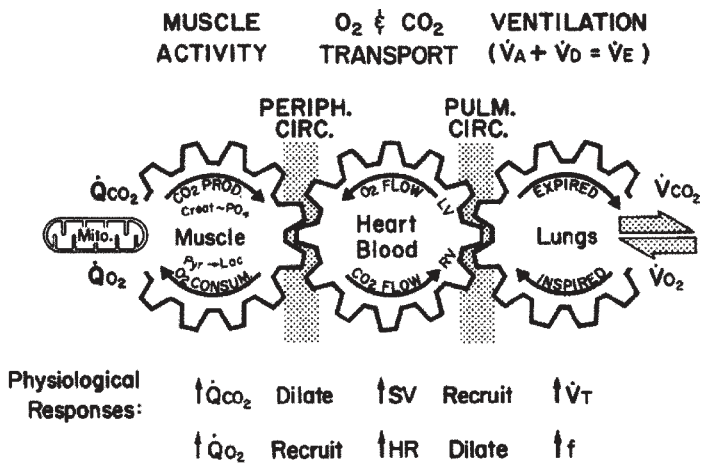


Fig. 1. Gas transport mechanisms for coupling cellular to pulmonary respiration. The gears represent functional interdependence of the physiological components of the system. (Printed with permission from Wasserman K, Hansen JE, Sue DY, Casaburi R, Whipp BJ, Principles of Exercise Testing and Interpretation 1999, 3rd ed., Lipincott, Williams & Wilkins.)

required to meet increased oxygen demand (VO_2) and remove excess carbon dioxide production (VCO_2). This coupling of respiratory, cardiovascular, and muscle gas transport systems is illustrated in Fig. 1 (1). The physiologic reserve capacity of the cardiovascular and respiratory systems is significantly high enough that even if much of this capacity is lost, demands of daily living will be met adequately (2). Abnormalities of exercise performance may be influenced by diseases of the heart, lungs, pulmonary and peripheral circulation, hemoglobin, muscles and/or cytochrome systems (3). In this chapter, we will initially discuss various methods of cardiopulmonary testing, and later we will discuss its applications in patients undergoing lung volume reduction surgery.

BROAD OVERVIEW OF METHODS OF CARDIOPULMONARY EXERCISE TESTING

Exercise testing allows the objective measurement of exercise capacity that can be compared with the ideal exercise capacity corrected for age, gender, height, and weight. In addition, symptoms that limit exercise can be elucidated and the physiologic responses to exercise can be analyzed in order to highlight patterns suggesting underlying organ dysfunction. Unfortunately, there is a lack of standardization concerning

the performance of clinical exercise testing (2). This applies to the methods used, variables being measured, and interpretive techniques. There are a number of predicted formulas that can be used to calculate the maximum VO_2 , work rate, heart rate, and minute ventilation (1,2,4). Exercise tests can be noninvasive, symptom limited, steady state, performed with arterial blood sampling, or with the presence of a pulmonary artery catheter (2). In addition, the tests can be conducted on various types of equipment: treadmill, cycle ergometer, step testing, or using an arm ergometer. The tests can be performed on room air or on supplemental oxygen. Using an electrically braked cycle ergometer leads to a more predictable increase in oxygen uptake than with a treadmill (2), using a treadmill results in an approx 7 % higher oxygen consumption than a cycle (5), increases in ventilation and blood lactate levels tend to be higher in cycling (6). The work performed on a treadmill is dependent on the weight of the subject, but this is not as significant with the cycle ergometer (7).

SAFETY ISSUES IN CARDIOPULMONARY EXERCISE TESTING

The safety of exercise testing has been well established and the risks to the patient are very small as long as simple precautions are observed. The risk of a myocardial infarction (MI) or serious arrhythmia is estimated at 1/10 000 submaximal tests (8), increasing to 1/2500 maximal tests if the patient has a history of MI (9). We feel that the test should be supervised by an experienced physician who is familiar with the patient's history and physical examination, and who is knowledgeable in resuscitative techniques. Before 1980, exercise tests were supervised by physicians 90% of the time. However, over the past 15 yr, cost containment initiatives have encouraged more extensive use of specially trained health professionals (nurses, exercise physiologists, physician assistants, and physical therapists) (10–12).

Absolute contraindications to exercise testing

1. The presence of an acute febrile illness.
2. EKG features of myocardial ischemia.
3. Uncontrolled heart failure.
4. Pulmonary edema.
5. Unstable angina.
6. Acute myocarditis.
7. Uncontrolled hypertension (> 250 mm systolic, 120 mm diastolic).
8. Uncontrolled asthma (2).

Relative contraindications to exercise testing

1. Recent (less than 4 wk previously) MI.
2. Aortic valve disease.
3. Resting tachycardia (HR >120/min).
4. Resting EKG abnormalities.
5. Poorly controlled diabetes.
6. Poorly controlled epilepsy.
7. Cerebrovascular disease.
8. Respiratory failure (2).

SPECIFIC ISSUES RELATING TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND EMPHYSEMA

Chronic obstructive pulmonary diseases (COPD) are characterized by reduced maximal expiratory flow and include various disease entities such as chronic obstructive bronchitis, asthmatic bronchitis, and emphysema. At least 14 million people in the United States suffer from COPD, and the prevalence of this disease seems to be increasing (13–16). As many as 2 million people suffer from emphysema, and the overall death rate for emphysema in the United States has been estimated at 20 000/yr, the fifth leading cause of death in North America (13,16–18). Exercise testing in patients with COPD has been stimulated by the increasing numbers of patients entering pulmonary rehabilitation programs (19), in addition to the availability of specific treatments for this condition, i.e., pulmonary transplantation and lung volume reduction surgery (LVRS).

TYPES OF CARDIOPULMONARY EXERCISE TESTING FOR PATIENTS WITH COPD

The simplest validated exercise test is the 6-min walk test performed either on or off oxygen. The inability to walk at least 200 m during this test has been shown to correlate with increased postoperative mortality (20). Patients with severe COPD present a number of difficulties when an incremental exercise test is performed. Their exercise capacity is frequently extremely limited (21), it is therefore difficult to obtain sufficient physiologic data. The exercise duration can be improved, however, by using small increments in the exercise load (21) and by using supplemental oxygen. Currently, the National Emphysema and Treatment Trial (NETT) is comparing the efficacy of LVRS and maximal medical therapy. Exercise tolerance is an important outcome measure in the study and the exercise techniques used in the NETT trial could serve as a standardized way of performing an incremental exercise test in patients with severe COPD.

Patients are exercised on an electrically braked cycle ergometer, which has the capability for electronic computer control to provide ramp workloads as low as 5 W/ min. The test is initially performed with arterial blood sampling, whereas subsequent tests during the trial may or may not use arterial sampling. The exercise tests are performed on an FIO₂ of 30%, the patients breathing in the O₂ and air mixture delivered from a high-flow blender to a large Douglas bag (>30 L). After being connected to the exercise equipment and getting on the cycle ergometer, the patient is observed for 5 min at rest, 3 min at 0 W cycling, and subsequently during a symptom-limited incremental exercise test (5 W/ min increments) (22). Exercise is considered maximal if one or more of the following criteria are met:

1. The patient's predicted maximal VO₂ is reached.
2. A clinically significant EKG abnormality develops.
3. Serum lactate increases to greater than 8 mmol/L.
4. Breathing reserve is less than 15 L /min.
5. The heart rate reserve is less than 10 beats/min.
6. The arterial PO₂ falls below 50 mmHg or the oxygen saturation falls below 84%.

The following parameters are measured:

1. Level of work (WR).
2. Heart rate (and the difference between heart rate and maximal predicted heart rate—the heart rate reserve).
3. EKG.
4. Blood pressure.
5. Respiratory rate.
6. Tidal volume (and the tidal volume to inspiratory capacity ratio).
7. Minute ventilation (VE) (and the difference between VE and maximal voluntary ventilation—the breathing reserve).
8. Oxygen consumption (VO₂), carbon dioxide production (VCO₂), and the relationship of these measures to the minute ventilation (VE/VO₂ and VE/VCO₂).
9. The VO₂/WR relationship.
10. The VO₂/heart rate response—the oxygen pulse.

RESPONSES TO EXERCISE IN CHRONIC OBSTRUCTIVE LUNG DISEASE

The two main factors reducing exercise capacity in COPD/emphysema are the reduced ventilatory capacity and the increased ventilatory requirement (1). Other factors include exercise-induced hypoxemia, cardiac dysfunction, and deconditioning (23). Both airway obstruction

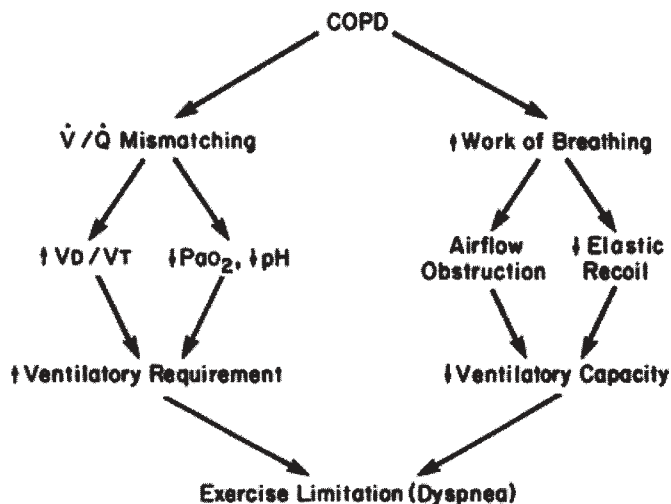


Fig. 2. Factors that play a role in exercise limitation and dyspnea in patients with chronic obstructive pulmonary disease. (Printed with permission from Wasserman K, Hansen JE, Sue DY, Casaburi R, Whipp BJ, Principles of Exercise Testing and Interpretation 1999, 3rd ed., Lipincott, Williams & Wilkins.)

and a reduction in lung elastic recoil are responsible for the decreased ventilatory capacity; the increased ventilatory requirements are a result of inefficient ventilation of the lungs because of mismatching of ventilation to perfusion (1) (Fig. 2). There is often a reduction in work that can be performed as a consequence of oxygen demand exceeding the maximal oxygen carrying capacity of the oxygen transport chain (21), and this is largely because of the failure of the available ventilatory reserve to meet the increasing ventilatory demands (24,25). The VO_2/WR response is often normal in patients with COPD, the oxygen cost of breathing, however, is much higher in COPD as compared to normal (21). There is a greater time constant for CO_2 excretion than O_2 consumption (50–60 s vs 30–40 s). Patients with COPD have increased numbers of lung units with high ventilation/perfusion ratios, these regions receiving up to 50% of blood flow, further exacerbating the delay in CO_2 output. The ventilatory response to exercise is dependent on the metabolic rate, the “set point level of arterial CO_2 ” and the wasted ventilation fraction (VD/Vt). The required minute ventilation at any given time may be calculated using the following equation:

$$VE = (863 \times VCO_2) / (PACO_2 \times (1 - VD/Vt))$$

with the arterial pCO_2 ($PaCO_2$) generally being substituted for the alveolar CO_2 ($PACO_2$) (21,26). Patients with stable COPD regulate

PaCO_2 at a reasonably constant level despite increasing work rates, in patients with severe COPD, however, the PaCO_2 may increase with exercise, worsening exercise-associated acidosis (1). Minute ventilation is frequently increased at rest in addition to being increased for a given level of exercise (1,21). This is frequently a result of the increased VD/V_t ratio, requiring an abnormal level of ventilation to maintain a normal PaCO_2 (27).

Many patients with COPD are hypoxemic, either at rest and/or during exercise. The degree of widening of the alveolar-arterial oxygen gradient with exercise is related to the degree of ventilation perfusion mismatching, particularly in regions of low ventilation/perfusion ratios (21).

DYNAMIC HYPERINFLATION AND ITS CONSEQUENCES

In patients with chronic lung diseases, the tidal volume tends to be lower and the respiratory rate tends to be higher at a given level of VE. A close relationship has been noted between measured vital capacity and maximal tidal volume during exercise (1,21). In patients with COPD, flow rates can be shown to reach the envelope of the resting maximal flow volume curve, which may contribute to exercise limitation (28,29). Normal subjects increase respiratory rate by decreasing inspiratory time (T_i) fractionally less than expiratory time (T_e)—as a consequence, the inspiratory duty cycle ($T_i/\text{total respiratory time}$) increases. In contrast, patients with COPD often show no increase in the inspiratory duty cycle, preserving greater time for exhalation. This is achieved by increasing inspiratory flow rates. There is, however, an associated increase in intrathoracic gas volume as a consequence of airflow limitation and increased respiratory frequency, eventually leading to a point on the thoracic cage pressure/volume relationship where inspiratory muscles function inefficiently, eventually leading to a large increase in thoracic gas volume with resultant fall in inspiratory flow (21,30). During exercise, the development of dynamic hyperinflation with a progressive increase in end-expiratory lung volume (EELV) imposes an additional elastic load on the ventilatory system, resulting in a reduction in inspiratory capacity, and is closely related to exertional dyspnea (31–33). This is in contrast to normal subjects in whom the EELV decreases with exercise (33). Traditionally, the maximal voluntary minute ventilation (MVV) (or multiple of the FEV1) has been compared to the maximal VE as an estimate of ventilatory capacity. Measuring the MVV in patients with COPD has shortcomings, however. Significant differences exist in the breathing patterns during the 12–15 s MVV maneuver and the breathing patterns during heavy exercise (33).

Ventilatory capacity can vary during exercise because of bronchodilation or bronchoconstriction, and is dependent on the lung volume where the tidal breathing occurs relative to the total lung capacity (TLC) and residual volume (RV). Measurements of the resting inspiratory capacity have been shown to closely correlate with maximal work in COPD patients (34). Breathing at higher lung volumes increases the inspiratory elastic load and, consequently, the work of breathing. Breathing at low lung volumes limits the available ventilatory reserve because of encroachment on the flow volume envelope. Reducing the total lung volume and residual volume, either medically by the use of bronchodilators (medical volume reduction) or surgically (surgical volume reduction), may indeed offer significant benefits by reducing EELV and subsequently availing more inspiratory capacity.

The technique of measuring the exercise inspiratory capacity, which allows superimposition of the exercise tidal volume loop on the maximal flow volume loop allows measurement of the EELV and the end inspiratory lung volume during exercise. This analysis provides more useful information about the cause of ventilatory limitation than analysis of the breathing reserve and breathing pattern (tidal volume and respiratory rate relationship) alone (33). Fig. 3 represents flow volume loops during exercise and compares the pattern in a healthy young male to that in a patient with emphysema.

CARDIOVASCULAR RESPONSE TO EXERCISE IN COPD PATIENTS

Patients with COPD can have coexisting cardiovascular diseases, because smoking is a risk factor for both COPD and ischemic heart disease and hypoxia can exacerbate ischemic heart disease. In patients with COPD, increases in cardiac output with exercise is less in comparison with normal subjects (35). Possible explanations for this phenomenon include cardiac dysfunction and elevations in pulmonary artery pressure with exercise due as a result hypoxia and or capillary destruction or obstruction, even in the absence of cor pulmonale (21,35,36).

EFFICACY OF LVRS

LVRS has been shown to significantly improve forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), and MVV, in addition to RV and TLC (37). Furthermore, lung elastic recoil has been shown to increase significantly after LVRS (38). The exercise capacity of patients with emphysema is thought to be determined by the mechanical constraints placed on maximal ventilation (39). Therefore, improvements in lung

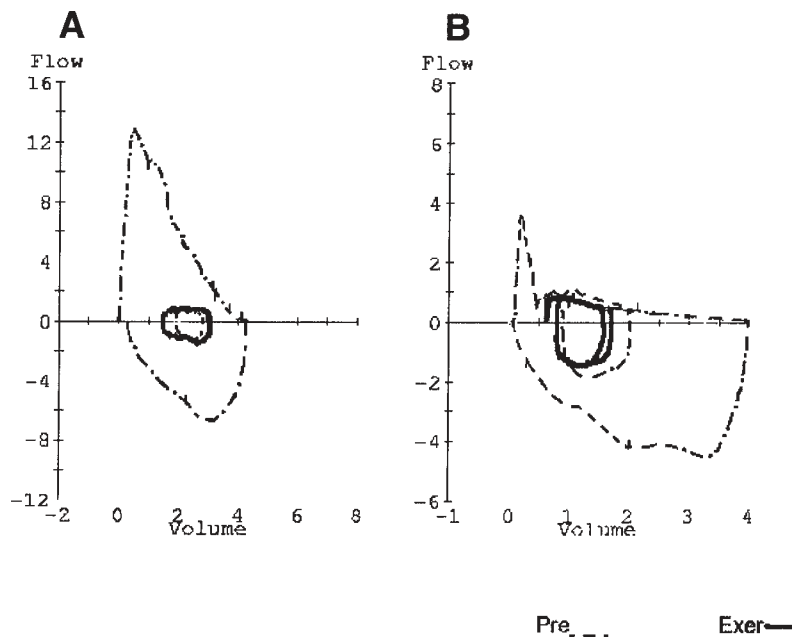


Fig. 3. Exercise flow volumes pre- and during exercise. Graph A represents the normal increase in tidal volume with exercise associated with a reduction in the end expiratory lung volume accompanied by an increase in the end inspiratory lung volume and no encroachment on the maximal resting flow volume loop. Graph B represents a patient with COPD, with an exercise-associated increase in the EELV. In addition, there is encroachment on the expiratory component of the maximal pre-exercise flow volume loop.

mechanics may explain the improvements noted following LVRS, specifically, the combination of the reduction in pulmonary hyperinflation, reduction in breathing frequency, reduction in mechanical constraints on tidal volume and reduction in functional residual capacity (FRC) (40). Improvements in exercise tolerance following LVRS include longer 6-min walk distances, increased maximal workloads, higher maximal VO_2 , and improved indices of gas exchange (41). Currently in the NETT trial, the 6-min walk test, maximal VO_2 , and maximum work rate are measured, with the maximum work rate as one of two primary outcomes to be analyzed (13,23,42–45).

Significant increases in the 6-min walk test have been noted following LVRS, from 300 to 370 m in normocapnic patients, and from 197 to 274 m in hypercapnic patients. The maximal VO_2 has also been shown to significantly increase in both normocapnic and hypercapnic patients following LVRS, from 14.6 to 17.02 mL/Kg/min and

11.7 to 14.7 mL/Kg/min, respectively (37). The same study also noted significant increases in the maximal V_t (0.85 to 1.05 L and 0.8 to 1.2 L, respectively, in normocapnic and hypercapnic patients); similarly, maximal minute ventilation increased from 29.2 to 33.5 L/min in normocapnic and 22.5 to 31 L/min, respectively, in hypercapnic patients (37).

The role of cardiovascular adaptations and altered heart–lung interactions in the improvements noted following LVRS is unclear. Most patients with severe emphysema have mild to moderate pulmonary hypertension, which may contribute to their exercise limitation (46). The consequences of LVRS on the pulmonary circulation are felt to be twofold: 1) resection of emphysematous lung tissue could reduce the vascular bed and increase pulmonary vascular resistance; and 2) better mechanical properties of the respiratory system with improved elastic recoil and less dynamic hyperinflation might counteract this effect and lead to a decrease in pulmonary vascular resistance (43,47). Strong correlations have been noted between improvements in gas exchange (the alveolar-arterial gradient) and reductions in mean exercise pulmonary artery pressure following ARDS, although these associations were not evident at rest (47,48). Other investigators have shown a trend to improvement in the VD/V_t ratio following LVRS (44). It is of interest that close correlations have been previously noted between the cardiac output and maximal $\dot{V}O_2$ at maximal exercise in patients with predominant cardiac dysfunction or pulmonary vascular disease. It is a possibility, therefore, that the increased $\dot{V}O_2$ noted following LVRS could, in part, represent an improvement in cardiac output (48,49). A strong association has been noted between the increases in FEV1 and the improvements in $\dot{V}O_2$ following LVRS (47,48). Thus it appears that there is a dichotomy between improvement in maximal $\dot{V}O_2$ and PaO_2 following LVRS. The former depends on improvements in FEV1, whereas the latter depends on improvement in pulmonary artery pressure.

LVRS has been shown to produce significant improvement in relief of dyspnea in many patients (44) in addition to improved quality-of-life scores (50). These improvements are generally associated with improvements in pulmonary function and exercise tolerance. However, the exact mechanism for the improvement in dyspnea is not precisely defined (50). Exercise testing before and after LVRS, including the use of the exercise flow volume loop and, in selected circumstances, invasive hemodynamic exercise testing will continue to improve our knowledge and help to ascertain the nature and duration of improvement in these patients. Moreover, as additional information is obtained from ongoing

clinical trials, the exercise test will help to define which patients are suitable candidates for the procedure (37).

REFERENCES

1. Wasserman K, Hansen JE, Sue DY, Casaburi R, Whipp BJ (1999) In: *Principles of Exercise Testing and Interpretation* 3rd ed. Lipincott, Williams & Wilkins, Baltimore, Maryland.
2. Jones NL, Moran Campbell EJ (1982) *Clinical Exercise Testing*, 2nd ed. Philadelphia, Pennsylvania: W. B. Saunders Co.
3. Goldring RM (1984) Specific defects in cardiopulmonary gas transport, *Am Rev Respir Dis* 129 (Suppl): S57–S59.
4. Blackie SP, Fairburn MS, McElvaney GN, Morrison NJ, Wilcox PG, Pardy RL (1989) Prediction of maximal oxygen uptake and power during cycle ergometry in subjects older than 55 years of age. *Am Rev Respir Dis* 139: 1424–1429.
5. Shephard RJ (1971) Standard tests of aerobic power, In: Shephard RJ, ed, *Frontiers of Fitness*. Springfield, IL: Charles C Thomas.
6. Shephard RJ (1966) The relative merits of the step test, bicycle and treadmill in the assessment of cardiorespiratory fitness. *Int Z Angew Physiol* 23: 219–230.
7. Wasserman K, Whipp BJ (1975) Exercise physiology in health and disease. *Am Rev Respir Dis* 112: 219–249.
8. Rochmis P, Blackburn H (1971) Exercise tests, a survey of procedures, safety and litigation experience in approximately 170,000 tests. *JAMA* 17: 1061–1066.
9. Shephard RJ (1970) For exercise testing - a review of procedures available to the clinician. *Bull Physiopathol Resp* 6: 425–474.
10. Franklin, BA, Gordon S, Timmis GC, O'Neill W (1997) Is direct physician supervision of exercise stress testing routinely necessary. *Chest* 111: 262–265.
11. Stuart RJ Jr, Ellestad MH (1980) National survey of exercise testing facilities. *Chest* 77: 94–97.
12. Cahalin LP, Blessey, RL, Kummer D, et al (1987) The safety of exercise testing performed independently by physical therapists. *J Cardiopulm Rehabil* 7: 269–276.
13. Utz JP, Hubmayr RD, Deschamps C (1998) Lung volume reduction surgery for emphysema: out on a limb without a NETT (Review). *Mayo Clinic Proc* 3: 552–566.
14. Higgins MW, Thom T (1989) Incidence, prevalence, and mortality: intra and inter country differences. *Lung Biol Health Dis* 43: 23–43.
15. Petty TL (1997) A new national strategy for COPD. *J Respir Dis* 18:363–369.
16. Feinleib M, Rosenberg HM, Collins JG, Delozier JE, Pokras R, Chevarley FM (1989) Trends in COPD morbidity and mortality in the United States. *Am Rev Respir Dis* 140 (Suppl): S9–S18.
17. American Thoracic Society (1995) Standards for the diagnosis and care of patients with chronic obstructive lung disease. *Am J Respir Crit Care Med* 152(Suppl): S77–S120.
18. American Lung Society (1993) Lung disease data. New York : American Lung Association.
19. Lacasee Y, Wong E, Guyatt GH, King D, Cook DJ, Goldstein RS (1996) Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. *Lancet* 348: 1115–1119.
20. Szekely, LA et al. (1997) Preoperative predictors of operative morbidity and mortality in COPD patients undergoing bilateral lung volume reduction surgery. *Chest* 111: 550–558.

21. ERS Task Force (1997) Clinical exercise testing with reference to lung diseases: indications, standardization and interpretation strategies. *Eur Respir J* 10: 2662–2689.
22. The National Emphysema Treatment Trial Research research protocol.
23. Benditt, JO, Lewis S, Wood DE, Klima L, Albert RK (1997) Lung volume reduction surgery improves maximal O₂ consumption, maximal minute ventilation, O₂ pulse, and dead-space-to-tidal volume ratio during leg cycle ergometry. *Am J Respir Crit Care Med* 156: 561–566.
24. Cooper JD, Patterson AG (1996) Lung volume reduction surgery for severe emphysema. *Semin Thorac Cardiovasc Surg* 8(1): 52–60.
25. Yusen, RD, Trulock EP, Pohl MS, Biggar DG, et al. (1996) Results of lung volume reduction surgery in emphysema. *Semin Thorac Cardiovasc Surg* 8(1): 99–1090.
26. Weisman IM, Zeballos RJ, eds. (1994) An integrated approach to the interpretation of the CPET, Clinical exercise testing in Clinics in Chest Medicine Philadelphia: W.B. Saunders.
27. Wagner PD, Gale GE. Ventilation perfusion relationships. In: Whipp BJ, Wasserman K, eds. Pulmonary physiology and pathophysiology of exercise. New York: Dekker, 1991; 121–142.
28. Potter WA, Olafsson S, Hyatt RE (1971) Ventilatory mechanics and expiratory flow limitation during exercise in patients with obstructive lung disease. *J Clin Invest* 50: 910–919.
29. Gallagher C (1990) Exercise and chronic obstructive pulmonary disease. *Med Clin N Am* 74: 619–641.
30. Jones NL, Berman LB (1984) Gas exchange in chronic air-flow obstruction. *Am Rev Respir Dis* 129 (Suppl): S81–S83.
31. Dodd DS, Brancatisano T, Engel LA (1988) Chest wall mechanics during exercise in patients with severe chronic air flow obstruction. *ARRD* 129: 33–38.
32. O'Donnell DE, Webb KA (1993) Exertional breathlessness in patients with chronic airflow limitation. *ARRD* 148:1351–1357.
33. Johnson BD, Weisman IM, Zeballos RJ, Beck KC (1999) Emerging concepts in the evaluation of ventilatory limitation during exercise - the exercise flow volume loop. *Chest* 116: 488–503.
34. Murariu C, Ghezzi H, Milic-Emili J, Gautier H (1998) Exercise limitation in obstructive lung disease. *Chest* 114: 965–968.
35. Stewart RI, Lewis CM (1986) Cardiac output during exercise in patients with COPD. *Chest* 89: 199–205.
36. Agusti AG, Barbera JA, Roca J, Rodriguez-Roisin R, Wagner PD, Agust-Vidal A (1990) Hypoxic vasoconstriction and gas exchange during exercise in chronic obstructive pulmonary disease. *Chest* 97: 268–275.
37. O'Brien GM, Furukawa S, Kuzma, AM, Cordova F, Criner GJ (1999) Improvements in lung function, exercise and quality of life in hypercapnic COPD patients after lung volume reduction surgery. *Chest* 115: 75–84.
38. Gelb AF, Brenner M, McKenna R, Fischel R, Zamel N, Schein MJ (1998) Serial lung function and elastic recoil 2 years after lung volume reduction surgery for emphysema. *Chest* 113: 1497–1506.
39. Potter WA, Olafsson S, Hyatt RE (1971) Ventilatory mechanics and expiratory flow limitation during exercise in patients with obstructive lung disease. *J Clin Invest* 50: 910–919.
40. O'Donnell DE, Webb KA, Bertley JC, et al. (1996) Mechanisms of relief of exertional breathlessness following unilateral bullectomy and lung volume reduction surgery in emphysema. *Chest* 110: 18–27.

41. Gelb AF, McKenna RJ, Brenner M, Schein MJ, Zamel N, Fischel R (1999) Lung function 4 years after lung volume reduction surgery for emphysema. *Chest* 116: 1608–1615.
42. The National Emphysema Treatment Trial Research Group (1999) Rationale and Design of the National Emphysema Treatment Trial, A Prospective Randomized Trial of Lung Volume Reduction Surgery. *Chest* 116: 1750–1761.
43. Sciurba FIC, Rogers RM, Keenan RJ, Silvka WA, Gorcsan J III, Ferson PF, et al (1996) Improvement in pulmonary function and elastic recoil after lung volume reduction surgery for diffuse emphysema. *N Engl J Med* 334: 1096–1099.
44. Keller CA, Ruppel G, Hibbett A, Osterloh J, Naunheim KS (1997) Thoracoscopic lung volume reduction surgery reduces dyspnea and improves exercise capacity in patients with emphysema. *Am J Respir Crit Care Med* 156: 60–67.
45. The National Emphysema Treatment Trial Research Group (1999) Rationale and design of the national emphysema treatment trial (NETT): a prospective randomized trial of lung volume reduction surgery. *J Thorac Cardiovasc Surg* 118: 518–528.
46. Light RW, Mintz HM, Linden GS, Brown SE (1984) Hemodynamics of patients with severe chronic obstructive pulmonary disease during progressive upright exercise. *Am Rev Respir Dis* 130: 391–395.
47. Oswald-Mammosser M, Kessler R, Massard G, Wihlm J, Weitzenblum E, Lonsdorfer J (1998) Effect of lung volume reduction surgery on gas exchange and pulmonary hemodynamics at rest and during exercise. *Am J Respir Crit Care Med* 158: 1020–1025.
48. Wagner PD (1998) Functional consequences of lung volume reduction surgery for COPD (Editorial). *Am J Respir Crit Care Med* 158: 1017–1019.
49. Balfe DL, Nathanson A, Wasserman K, Mohsenifar Z. Does pulmonary artery catheterization add to traditional cardiopulmonary exercise testing in diagnosing dyspnea? submitted for publication.
50. Cooper JD, Trulock EP, Triantafillou AN, Patterson GA, Pohl MS, Deloney PA, Sundaresan RS, Poper CL (1995) Bilateral pneumonectomy (volume reduction) for chronic obstructive pulmonary disease. *J Thorac Cardiovasc Surg* 109:106–119.



<http://www.springer.com/978-0-89603-848-6>

Lung Volume Reduction Surgery
Argenziano, M.; Ginsburg, M.E. (Eds.)
2002, XII, 274 p., Hardcover
ISBN: 978-0-89603-848-6
A product of Humana Press