# EXERCISE TESTING IN ASSESSMENT AND MANAGEMENT OF PATIENTS IN CLINICAL PRACTICE - PRESENT SITUATION

#### Sumer S Choudhary, Sanjiw Choudhary

Lung India 2008; 25 : 111-117

\_

Key words : Exercise; heart; Interpretation; methodology; 6min walk test; testing

## **OBJECTIVE**

- 1) To review recent scientific advances in exercise testing methods and results that is important for a clinical practioner.
- 2) To understand the utility and limitations of different methods of exercise testing.
- 3) To understand appropriate method in assessment and management of patients.
- 4) To appreciate that exercise testing results can have greater clinical meaning when interpreted in context of relevant patient information.
- 5) To understand that additional study is required to further characterize both current and future roles of exercise testing in clinical medicine.

### **INTRODUCTION**

The need of the hour is to understand the different methods used worldwide to asses the patients exercise performance and response in clinical practice.

Clinical Exercise Testing (CET) is increasingly gaining importance in clinical medicine, by helping the clinician to objectively evaluate the physiological functions. The result helps to predict the outcome and mortality in different clinical circumstances.

# COMMON METHODS TO ASSES EXERCISE RESPONSE AND PERFORMANCES IN CLINICAL PRACTICE

Simple test are easily performed but limits physiological understanding.

More comprehensively performed tests may provide detail information and understanding but is costly and demanding. The clinician has to choose the type of test to perform for a particular patient. Commonly the following test is performed worldwide:-

- 1) 6 min walk test
- 2) Shuttle Walk Test
- 3) Exercise Induced Bronchoconstriction Test
- 4) Cardiac Stress Test
- 5) Clinical Exercise Test (CET)

#### **6 MINUTE WALK TEST**

It is a safe simple and practical test of sub maximal functional capacity, which measures the maximum distance walked by a subject in 6 minutes. Advantage of this test is that it provides an acceptable index of functional disability and correlates with oxygen uptake measured during comprehensive testing. This test gives very limited information regarding physiological contributors to activity related symptoms or about mechanism of exercise limitation. Currently this test is used in lung transplantation, lung volume reduction surgery, pulmonary rehabilitation and in predicting mortality in cardiac patients and patients with pulmonary vascular disorders.

## SHUTTLE WALK TEST

It measures the distance walked by a patient in a 10 meter course, being paced by an audio signals from a cassette. The intensity of exercise reached is comparable to test performed on a treadmill, as the walking speed is progressively increased until the patient reaches exhaustion. Modification of maximal SWT for determination of endurance performance – similar to maximal and constant (sub maximal) cycle ergometry may be done.

# EXERCISE INDUCED BRONCHOCONSTRICTION

In this physical activity triggers acute airway narrowing in patients with heightened airway responsiveness. In susceptible patients EIB typically occurs 5to 10 minutes

Department of Pulmonary Medicine, Sleep Medicine, Critical Care, Shree Ramjevan Choudhary Memorial Hospital and Research Centre, Nagpur, Maharashtra, India. *Correspondence :* Dr. Sumer S. Choudhary, Shree Ramjevan Choudhary Memorial Hospital and Research Centre, Choudhary Road, Nagpur - 02.

Received : October 2007 Accepted : December 2007

after exercise. and generally resolves in 20 to 30 minutes. In some clinical situation where bronchial challenge is unavailable or not diagnostic EIB should be undertaken.

Common protocols to be followed include exercise on treadmill or cycle ergometry at a workload of 60 % to 80% of predicted maximum or the intensity that will elicit a heart rate of 80% of predicted maximum for 6 to 8 minutes. The goal is to produce ventilation equal to those attained during activity to produce symptom of EIB.

15% percent decrease in  $\text{FEV}_1$  following exercise is diagnostic of EIB.And 10-15 % decrease in  $\text{FEV}_1$  would be suggestive of EIB.

# CARDIAC STRESS TEST

Common type of exercise testing, the primary purpose of which is diagnosis and management of myocardial infarction. Bruce protocol is commonly used and the single most reliable indication of ischemia is ST segment depression. During this test ECG and BP is measured, but the utility may be enhanced by concurrent measurement of ventilator parameters and respiratory gas exchange.

## CLINICAL EXERCISE TESTING (CET)

CET involves the measurement of respiratory gas exchange i.e. oxygen uptake, carbon dioxide , minute ventilation, other variables while monitoring ECG, blood pressure , pulse oximetry and exertion perceived (Borg Scale) during a maximal symptom limited incremental test on a cycle ergo meter or treadmill. Simultaneous measurement of blood gasses and spirometry provides with more detail information on gas exchange and ventilation.CET provides a global assessment of integrative exercise responses which are not adequately reflected by measurement of individual organ system function on rest. Peak oxygen uptake remains the gold standard for exercise capacity.

It has tradionaly been undertaken with an incremental stepwise or ramp control protocol to exhaustion. In patients of COPD, acute response to an inhaled bronchodilator was assessed using various exercise tests. The authors found endurance time with a constant – workload exercise (80% of maximal work rate)was the most responsive end point to the effect of bronchodilator showing 19% improvement in exercise duration time. Arterial blood gasses measured at 5 minute constant – work exercise testing may give practical and cost effective alternative when arterial oxygen saturation, PaO2, alveolar –arterial oxygen pressure difference and ratio of physiological dead space to tidal volume are required.

# INDICATIONS FOR EXERCISE TESTING IN CLINICAL PRACTICE

- 1. Evaluation of Exercise Intolerence
- 2. Evaluation of Unexplained exertional Dysponea

- 3. Evaluation of patients of cardiovascular diseases
- 4. Evaluation of Patients of respiratory diseases
  - COPD
  - ILD
  - Pulmonary Vascular Diseases
  - Cystic Fibrosis
- 5. Preoperative evaluation
- 6. Evaluation for transplantation and Lung Volume Reduction Surgeries
- 7. Pulmonary Rehabilitation
- 8. Impairment disability

Table 1 to 11 illustrates the indication, contraindication and guidelines laid down by various international authorities for cardio pulmonary exercise testing in clinical setting.

### CONCLUSION

Cardiopulmonary exercise test is a helpful tool for evaluation of the disease and management in clinical practice and rapidly evolving in one of the important investigative and diagnostic test. There are different methods used in various clinical setting. The clinical exercise testing a simple and easy to perform test for a pulmonologist as compared to the other conducted tests and relatively more simpler and cost effective test, which needs to be more frequently used in our day to day clinical practice in relevant patients.

#### Table I : Overview of Cardiopulmonary Exercise Testing

#### **Clinical Status Evaluation**

Clinical diagnosis and reason(s) for CPET Health questionnaire (cardiopulmonary); physical activity profile Medical and occupational history and physical examination PFTs, CXR, ECG, and other appropriate laboratory tests. Determination of indications and contraindications for CPET

### Ť

#### **Pretest Procedures**

Abstain from smoking for at least 8 h before the test Refrain from exercise on the day of the test Medications as instructed Consent form

### ţ

#### **Conduct of CPET**

Laboratory procedures Quality control Equipment calibration Protocol Selection Incremental versus constant work rate; invasive versus nominvasive Patient preparation Familiarization 12-lead ECG, pulse oximetry, blood pressure Arterial line (if warranted)

Cardiopulmonary exercise testing

### Interpretation of CPET Results

#### Data processing

Quality and consistency of results Comparison of results with appropriate reference values Integrative approach to interpretation CPET results Preparation of CPET report

Definition of abbreviations : CPET = Cardiopulmonary exercise testing; CXR = chest X-ray; ECG ; electrocardiogram; PFTs = pulmonary function tests.

#### Table II : Indications for Cardiopulmonary Exercise Testing

#### Evaluation of exercise tolerance

- Determination of functional impairment or capacity (peak Vo<sub>2</sub>)
- Determination of exercise-limiting factors and pathophysiologic mechanisms.

#### Evaluation of undiagnosed exercise intolerance

- Assessing contribution of cardiac and pulmonary etiology in coexisting disease.
- Symptoms disproportionate to resting pulmonary and cardiac tests.
- Unexplained dyspnea when initial cardiopulmonary testing is nondiagnostic.

#### Evaluation of patients with cardiosvascular disease

- Functional evaluation and prognosis in patients with heart failure
- Selection for cardiac transplantation
- Exercise prescription and monitoring response to exercise training for cardiac rehabilitation.

(special circumstance; i.e. pacemakers)

#### Evaluation of patients with respiratory disease

- Functional impairement asessment (see specific clinical applications)
- Chronic obstructive pulmonary disease

Establishing exercise limitation(s) and assessing other potential contributing factors, especially occult heart disease (ischemia)

Determination of magnitude of hypoxemia and for  $\mathrm{O_2}$  prescription

When objective determination of therapeutic intervention is necessary and not adequately addressed by standard pulmonary function testing.

• Interstitial lung diseases

Detection of early (occult) gas exchange abnormalities

Overall assessment/ monitoring of pulmonary gas exchange

Determination of magnitude of hypoxemia and for  $\mathrm{O_2}$  prescription

Determination of potential exercise-limiting factors

Documentation of therapeutic response to potentially toxic therapy

- Pulmonary vascular disease (careful risk-benefit analysis required)
- Cystic fibrosis
- Exercise-induced bronchospasm

#### Specific clinical applications

- Preoperative evaluation
   Lung resectional surgery
   Elderly patients undergoing major abdominal surgery
   Lung volume resectional surgery for emphysema (currently investigational)

   Exercise evaluation and prescription for pulmonary
- Exercise evaluation and prescription for pulmonary rehabilitation
- Evaluation for impairment-disability
- Evaluation for lung, heart-lung transplantation

Reference 20	Definition of abbreviations :	Vo <sub>2</sub> = oxygen consumption Reference 20
--------------	-------------------------------	--

# Table III : Absolute and Relative Contraindications forCardiopulmonary Exercise Test

	Absolute	Relative			
	Acute myocardial infarction (3-5 days)	Left main coronary stenosis or its equivalent			
	Unstable angina	Moderate stenotic valvular heart disease			
	Uncontrolled arrhythmias causing symptoms or hemodynamic compromise	Severe untreated arterial hyper- tension at rest (> 200 mm Hg systolic, > 120 mm Hg diastolic)			
	Syncope	Tachyarrhythmias or bradyarrhy- mias			
	Active endocardities	High-degree atrioventricular block			
	Acute myocarditis or pericarditis	Hypertrophic cardiomyopathy			
	Symptomatic severe aortic stenosis	Significant pulmonary hypertension			
	Uncontrolled heart failure	Advanced or complicated pregnancy			
	Acute pulmonary embolus or pulmonary infarction	Electrolyte abnormalities			
	Thrombosis of lower extremities	Orthopedic impairment that compromises exercise performance			
	Suspected dissecting aneurysm				
	Uncontrolled asthma				
	Pulmonary edema				
Room air desaturation at rest < 85%*					
	Respiratory failure				
	Acute noncardiopulmonary disorder that may affect exercise performance or be aggrevated by exercise (i.e. infection, renal failure, thyrotoxicosis)				
	Mental impairment leading to inability to cooperate				

References 21, 22 and 23.

\* Exercise patient with supplemental O<sub>2</sub>.

#### Table IV: Indications for Exercise Termination

Chest pain suggestive of ischemia
Ischemic ECG changes
Complex ectopy
Second or third degree heart block
Fall in systolic pressure > 20 mm Hg from the highest value during the test
Hypertension (> 250 mm Hg systolic; > 120 mm Hg diastolic)
Severe desaturation : Spo <sub>2</sub> < 80% when accompanied by symptoms and signs of severe hypoxemia
Sudden pallor
Loss of coordination
Mental confusion
Dizziness or faintness
Signs of respiratory failure

Definition of abbreviations : ECG = electrocardiogram;  $Spo_2 = arterial oxygen saturation as indicated by pulse oximetry. References 22, 24, 25 and 26.$ 

				Pulmonary		
Measurement	Heart Failure	COPD	ILD	Vascular Disease	Obesity	Deconditioned
Vo <sub>2</sub> max or Vo <sub>2</sub> peak	Decreased	Decreased	Decreased	Decreased	Decreased for actual, normal for ideal weight	Decreased
Anaerobic threshold	Decreased	Normal/decreased indeterminate	Normal or decreased	Decreased	Normal	Normal or decreased
Peak HR	Variable, usually normal in mild	Decreased, normal in mild	Decreased	Normal/slightly decreased	Normal/slightly decreased	Normal/slightly decreased
O <sub>2</sub> pulse	Decreased	Normal or decreased	Normal or increased	Normal	Normal or increased	Normal
(VE/MVV) x 100	Normal or decreased	Increased	Increased	Increased	Normal	Normal
VE/Vco <sub>2</sub> (at AT)	Increased	Increased	Increased	Increased	Normal	Normal
VD/VT	Increased	Increased	Increased	Increased	Normal	Normal
Pao <sub>2</sub>	Normal	Variable	Decreased	Decreased	Normal/ may increase	Normal
P(A-a)O <sub>2</sub>	Usually normal	Variably, usually increased	Increased	Increased	May decrease	Normal

#### Table V: Usual Cardiopulmonary Exercise Response Patterns

Definition of abbreviations : AT = anaerobic threshold; COPD = chronic obstructrutive pulmonary disease; HR = heart rate; ILD = interstitial disease; MVV = maximal voluntary ventilation;  $P(A-a)O_2$  = alveolar-arterial difference for oxygen pressure; VD/VT = ratio of physiologic dead space to tidal volume; VE = minute ventilation;  $Vco_2$  = carbon dioxide output;  $Vo_2$  max = maximal oxygen uptake;  $Vo_2$  peak = peak oxygen uptake. References **37, 38** and **28** 

\* Decreased, normal, and increased are with respect to the normal response.

	16	1 •	<b>A</b> 1.	1	<b>r</b> •	
Table VI •	Measurements	during	Cardioni	ulmonary	Exercise	lesting
Table VI.	measurements	uuring	Carulop	unnonai y	LACICISC	resung

Measurements	Nominvasive	Invasive (ABGs)
External work	WR	
Metabolic gas exchange	Vo <sub>2</sub> , Vco <sub>2</sub> , RER, AT	Lactate
Cardiovascular	HR, ECG, BP, O <sub>2</sub> pulse	
Ventilatory	Va, Vr, fR	
Pulmonary gas exchange	Spo <sub>2</sub> , Vr/Vco <sub>2</sub> , Vr/Vo <sub>2</sub> , Рето <sub>2</sub> , Ретсо <sub>2</sub>	Pao <sup>2</sup> , Sao <sup>2</sup> , P(A-a)O <sub>2</sub> , VD/VT
Acid-base		pH, Paco², standard HCO <sub>3</sub>
Symptoms	Dyspnea, fatigue, chest pain	

Definition of abbreviations : ABGs = Arterial blood gases; AT = anaerobic threshold; BP = Blood pressure; ECG = electrocardiogram; fR = respiratory frequency; HR = heart rate;  $P(A-a)O_2$  = alveolar-arterial difference for oxygen pressure;  $Paco_2$  = arterial carbon dioxide pressure;  $Pao_2$  = arterial oxygen pressure;  $PeT-co_2$  = end-tidal  $Pco_2$ ;  $PETo_2$  = end-tidal  $Po_2$ ; RER = respiratory exchange ratio;  $Sao_2$  = arterial oxygen saturation as indicated by pulse oximetry;  $Vco_2$  = carbon dioxide output; VE = minute ventilation; VD/VT = ratio of physiologic dead space to tidal volume;  $Vo_2$  = oxygen uptake; VT = tidal volume; WR = work rate. **31** 

Variables	Criteria of Normality
Vo <sub>2</sub> max or Vo <sub>2</sub> peak	> 84% predicted
Anaerobic threshold	> 40% Vo <sub>2</sub> max predicted; wide range of normal (40-80%)
Heart rate (HR)	HRmax > 90% age predicted
Heart rate reserve (HRR)	HRR < 15 beats/min
Blood pressure	< 220/90
O <sub>2</sub> pulse (Vo <sub>2</sub> /HR)	> 80%
Ventilatory reserve (VR)	MVV - Vemax: > 11 or Vemax/MVV x 100 : < 85%. Wide normal range : 72 + 15%
Respiratory frequency (fR)	< 60 breaths/min
VE/ Vco <sub>2</sub> (at AT)	< 34
Vd/Vt	< 0.28; < 0.30 for age > 40 years
$Pao_2 > 80 \text{ mm Hg}$	
Р (а-а) О <sub>2</sub>	< 35 mm Hg

# Table VII : Suggested normal guidelines for interpretation of Cardiopulmonary Exercise Testing

References 27, 28, 30, 35, 22 and 32

\* Maximum or peak cardiopulmonary responses except for anaerobic threshold and Ve/Vco, at AT.

### Table VIII : Integrative approach to the interpretation of Cardiopulmonary exercise testing results

- 1. Determine reason(s) for CPET
- 2. Review pertinent clinical and laboratory information (clinical status)
- 3. Note overall quality of test, assessment of subject effort, and reasons for exercise cessation
- 4. Identify key variables: initially Vo<sub>2</sub>, and then HR, VE, Sao<sub>2</sub>, and other measurements subsequently.
- 5. Use tabular and graphic presentation of the data
- 6. Pay attention to trending phenomena : submaximal through maximal responses.
- 7. Compare exercise responses with appropriate reference values.
- 8. Evaluate exercise limitation : physiologic versus nonphysiologic.
- 9. Establish patterns of exercise responsess.
- 10. Consider what conditions / clinical entities may be associated with these patterns.
- 11. Correlae CPET results with clinical status.
- 12. Generate CPET report.

Definition of abbreviations : CPET = cardiopulmonary exercise testing; HR = heart rate; Sao<sub>2</sub> = arterial oxygen saturation; Ve = minute ventilation; Vo<sub>2</sub> = oxygen uptake. Reference 27

				Pulmonary		
Measurement	Heart Failure	COPD	ILD	Vascular Disease	Obesity	Deconditioned
Vo <sub>2</sub> max or Vo <sub>2</sub> peak	Decreased	Decreased	Decreased	Decreased	Decreased for actual, normal for ideal weight	Decreased
Anaerobic threshold	Decreased	Normal/decreased indeterminate	Normal or decreased	Decreased	Normal	Normal or decreased
Peak HR	Variable, usually normal in mild	Decreased, normal in mild	Decreased	Normal/slightly decreased	Normal/slightly decreased	Normal/slightly decreased
O <sub>2</sub> pulse	Decreased	Normal or decreased	Normal or increased	Normal	Normal or increased	Normal
(VE/MVV) x 100	Normal or decreased	Increased	Increased	Increased	Normal	Normal
VE/Vco <sub>2</sub> (at AT)	Increased	Increased	Increased	Increased	Normal	Normal
VD/VT	Increased	Increased	Increased	Increased	Normal	Normal
Pao <sub>2</sub>	Normal	Variable	Decreased	Decreased	Normal/ may increase	Normal
P(A-a)O <sub>2</sub>	Usually normal	Variably, usually increased	Increased	Increased	may decrease	Normal

#### Table IX : Cardiopulmonary Exercise Response Patterns

Definition of abbreviations : AT = anaerobic threshold; COPD = chronic obstructrutive pulmonary disease; HR = heart rate; ILD = interstitial disease; MVV = maximal voluntary ventilation;  $P(A-a)O_2$  = alveolar-arterial difference for oxygen pressure; VD/VT = ratio of physiologic dead space to tidal volume; VE = minute ventilation;  $Vco_2$  = carbon dioxide output;  $Vo_2$  max = maximal oxygen uptake;  $Vo_2$  peak = peak oxygen uptake. References 37, 36, 28

\* Decreased, normal, and increased are with respect to the normal response.

#### Table X :



Basic strategy for the interpretation of peak CPET results begins with consideration of patient information and reasons for testing and with analysis of  $Vo_2max$  and subsequently simultaneous assessment of HR, VE, and  $Sao_2$ . The AT may be helpful at this point. Determination of physiologic limitation is accomplished by analysis of ventilatory reserve (VE/MVV) and heart rate reserve (HRR). Additional CPET measurements and patterns of response are established and (likely) associated clinical entitles are considered, resulting in more specific diagnostic pathways (28). **CAD** = conronary artery disease.

# Table XI : Selected reference values for maximal incremental cycle exercise test

Variables	Equations*
Vo <sub>2</sub> , ml/min, male	W X [50.75 - 0.372 (A)]
Vo <sub>2</sub> , ml/min, female	(W - 43) x [22.78 - 0.17 (A)]
HR, beats/min	210 x 0.65 (A)*
O <sub>2</sub> pulse, ml/beat	Predicated Vo <sub>2</sub> max/predicted HRmax
Ve/MVV, %	~ 72 + 15
AT, L/min (Vo <sub>2</sub> )	> 40% Vo <sub>2</sub> pred

Definition of abbreviations : AT = Anaerobic threshold; HR = heart rate; Ve = minute ventilation; Vo<sub>2</sub> = oxygen uptake.

Data from Referenes 32, 33 and 34

\* Age (A) : years; height (H) : centimeters; weight (W), kilograms.

Predicted weight men :  $0.79 \times H - 60.7$ . Predicted weight women: 0.65 x H - 42.8. When actual weight > predicted, the predicted weight should be used in the equations. Wasserman and colleagues

introduced new corrections factors (34, 28), which have not yet been published in peer reviewed journals.

^ See Lange-Andersen and coworkers (345).

#### REFERENCES

- Criner GJ, Cordova FC, Furukawa S, et al. Prospective randomized trial comparing bilateral lung volume reduction surgery to pulmonary rehabilitation in sever chronic obstructive pulmonary disease. Am J Resp Crit Care Med 1999; 160:2018-2027.
- 2. Singh SJ, Morgan MD, Scott S, et al. Development of shuttle walking test of disability in patients with chronic airway obstruction. Thorax 1992; 47:1019-1024.
- Miyamoto S, Nagaya N, Satoh T, et al .Clinical correlates and prognostic significance of six minute walk test in patients with primary pulmonary hypertension: comparison with cardiopulmonary exercise testing. Am J Crypt Care Med 2000; 161:487-492.
- ATS committee on Proficiency Standards for clinical Pulmonary Function Laboratories. ATS statement: guidelines for six minutes walk test. Am J Crit Care Med 2002; 166:111-117.

- 5. Kadikar A, Maurer J, Kesten S. The six minute walk test: a guide to assessment for lung transplantation .J Heart Lung Transplant 1997; 16:313 -319.
- 6. Marciniuk DD ,Cockcroft DW. Exercise –induced bronchoconstriction: the role of leukotrienes modifiers in therapy. Can J Allergy Clin Immunol 1998; 3:298-303.
- Cahalin I, Pappagianopoulos P, Prevost S, et al. The relationship of 6 – minute walk to maximal oxygen consumption in transplant candidates with end stage lung disease. Chest 1995; 108: 452 -459.
- 8. Cypcar D, Lemanske RF. Asthama and exercise. Clin Chest Med; 156:351-368.
- 9. Bittener V, Weiner DH, Yusuf S, et al. Prediction of mortality and morbidity with a 6 min walk test in patients with left ventricular dysfunction.JAMA 1993; 270:1702-1707.
- Singh SJ,Morgan MD, Hardman AE, et al. Comparison of oxygen uptake during a conventional treadmill test and the walking test in chronic airflow limitation .Eur Respir J 1994; 7 2016-2020.
- 11. American Thoracic Society. Guidelines for methacholine and exercise challenge testing-1999 Am J Respir Crit Care Med 2000; 161:309-329.
- Gibbons RJ, Balady GJ, Beasley JW, et al. ACC/AHA guidelines for exercise testing: a report of the American College of Cardiology/American Heart Association Task Force on Practice guidelines (Committee on Exercise Testing), J AM Coll Cardiol 1997; 30: 260-315.
- 13. ZeballosRJ, Weisman IM, Connery SM. Comparison of pulmonary gas exchange measurements between incremental and constant work exercise above the anaerobic threshold. Chest 1998; 113:: 602 -611.
- 14. Oga T, Nishimura K, Tsukino M, et al. The effects of oxitropium bromide on exercise performance in patients with stable chronic obstructive pulmonary diseases. Am J Respir Crit Care Med 2000; 161: 1897-1901.
- Weisman IM, Zeballous RJ,eds Integrative approach to the interpretation of cardiopulmonary exercise testing. In: Weisman IM, Zealot RJ, eds. Clinical exercise testing. Basel, Switzerland: Karger. Prog Respir Res 2002:32: 300-322.
- Weisman IM, Beck K, Casaburi R, et al. American Thoracic Society/American College of Chest Physicians Joint statement on Cardiopulmonary Exercise Testing. Am J Respir Crit Care Med 2003; 167: 211-277.
- Beck KC, Weisman IM. Methods for Cardiopulmonary Exercise Testing. Weisman IM, Zeballos RJ, eds. Clinical exercise testing. Basel, Switzerland: Karger. Prog Respir Res 2002;32: 43-59.
- *18. Johnson BD, Weisman IM, Zeballos RJ, et al. Emerging concepts in the evaluation of ventilatory limitation during exercise. Chest 1999; 116:488-503.*
- Zeballos RJ, Weisman IM. Modalities of clinical exercise testing. In: Weisman IM, Zeballos RJeds. Clinical Exercise Testing. Basel Switzerland: Karger. Prog Respir Res 2002; 32:30-42.
- 20. Weisman IM, Zeballos RJ. Clinical exerscise testing. Pulm Crit Care Update 1995;11:1-9.

- 21. Fletcher GF, Balady G, Froelicdher VF, Hartley LH, Haskell WL, Pollock ML, Weisman IM, Exercisde standarda :a stsatement for healthcare professionals from the American heart association. Circulation 1995; 91:580-615.
- 22. Jones NL ,Clinical Exercise testing , 4th ed.1997, Philadelphia: W.B Saunders ; p.xi.
- 23. American College of sports Medicine. Guidelines for exercise testing and prescription, 4th ed. Philadelphia: Lea and Febiger;1991.p.xv.
- 24. Committee of exercise testing . ACC/AHA Guidelines for exercise testing :a report of the American College of Cardiology / American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 1997;30:907-912
- 25. American College of sports medicine .ACSM guidelines for exercise testing and prescription, 6th ed. Baltimore, MD: Williams and Wilkins; 200.p.xvi.
- 26. Lollgen H, Ulmer H-V, Crean P, editors. Recommendations and standard guidelines for exercise testing. Report of the task force Conference on ergometry, Titssee1987.Eur Heart J 1988; (9 Suppl K): 1-37.
- 27. Weisman IM, Zeballos RJ. An integrated approach to the interpretation of cardiopulmonary exercise testing. Clin Chest Med 1994; 15:421-445.
- 28. Wasserman K, Hansen JE, Sue DY, Whipp BJ, Casaburi r. Principles of exercise testing and interpretation including pathophysiology and clinical application, 3rd ed. Philadelphia:Lippincott Williams and Williams ;199.p.xv.
- 29. American college of sports medicine. ACSM guidelines for exercise testing and prescription, 5th .ed.Baltimore: Williams and Wilkins; 1995.p.xvi.
- 30. Sue DY, Hansen JE, Normal values in adults during exercise testing. Clin Chest Med 1984; 5 : 89-98.
- 31. Weisman IM, Zeballous RJ.Clinical exercises Testing. Clin Chest Med 2001; 22: 679-701.
- 32. Hansen Jed, Sue DY, Wasserman K. Predicted values for clinical exercise testing .Am Rev Respir Dis 1984; 129:s49-s55.
- *33.* Bruce RA, Kusumi F, Hosner D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease . Am Heart j 1973; 85:546-562.
- 34. Wasserman k, Hansen JE, Sue DY., Whipp BJ, Casaburi R, Principles of exercise testing and interpretation. Phildelphia :Lea and Febiger 1987. p. xiii.
- 35. American College Of sports medicine.ACSM guidelines for exercise testing and prescription, 5th ed .Baltimore.Williams and Wilkins; 1995.p.xvi.
- 36. Weisman IM, Zeballous RJ, Clinical evaluation of unexplained dyspnoea. Cardiologia 1996; 41:621-634.
- *37.* Gallagher CG.Exercise limitation and clinical exercise testing in chronic obstructive pulmonary disease.Clin Chest Med 1994; 15:305-326.
- *38.* ATS/ACCP statement on cardipulmonary exercise testing, Am J Respir Crit Care Med Vol 167 pp 211-277, 2003.