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# Cardio Pulmonary Exercise Test (CPET/CPX) in Cardiology

## General Guidelines

**ESC 2017: Role of cardiopulmonary exercise testing in clinical stratification in heart failure. A position paper from the Committee on Exercise Physiology and Training of the Heart Failure Association of the European Society of Cardiology.**

*Corrà U, Agostoni PG, Anker SD, Coats AJS, Crespo Leiro MG, de Boer RA, Hairola VP, Hill L, Lainscak M, Lund LH, Metra M, Ponikowski P, Riley J, Seferovi PM, Piepoli MF. Eur J Heart Fail. 2017 Sep 18.*

Traditionally, the main indication for cardiopulmonary exercise testing (CPET) in heart failure (HF) was for the selection of candidates to heart transplantation. Today, CPET is used in broader patients' populations, including women, elderly, patients with co-morbidities, those with preserved ejection fraction, or left ventricular assistance device recipients, i.e. individuals with different responses to incremental exercise and markedly different prognosis. Moreover, the diagnostic and prognostic utility of symptom-limited CPET parameters derived from submaximal tests is more and more considered, since many patients are unable to achieve maximal aerobic power. Repeated tests are also being used for risk stratification and evaluation of intervention, so that these data are now available. Finally, patients, physicians and healthcare decision makers are increasingly considering how treatments might impact morbidity and quality of life rather than focusing more exclusively on hard endpoints (such as mortality) as was often the case in the past. Innovative prognostic flowcharts, with CPET at their core, that help optimize risk stratification and the selection of management options in HF patients, have been developed.

## Useful Links

### COSMED Cardio Pulmonary Exercise Testing

<http://www.cosmed.com/cpet>

### COSMED Homepage

<http://www.cosmed.com>

**ESC 2016 Focused Update: Clinical Recommendations for Cardiopulmonary Exercise Testing Data Assessment in Specific Patient Populations**

*Guazzi M, Arena R, Halle M, Piepoli MF, Myers J, Lavie CJ. Eur Heart J. 2016 May 2.*

The purposes of this update are to confirm algorithms included in the initial scientific statement not requiring revision, to propose revisions to algorithms included in the initial scientific statement, to propose new algorithms based on emerging scientific evidence, to further clarify the application of oxygen consumption at ventilatory threshold, to describe CPX variables with an emerging scientific evidence base, to describe the synergistic value of combining CPX with other assessments, to discuss personnel considerations for CPX laboratories, and to provide recommendations for future CPX research.

**AHA 2016: Importance of Assessing Cardiorespiratory Fitness in Clinical Practice: A Case for Fitness as a Clinical Vital Sign: A Scientific Statement From the American Heart Association.**

*Ross R, Blair SN, Arena R, Church TS, Després JP, Franklin BA, Haskell WL, Kaminsky LA, Levine BD, Lavie CJ, Myers J, Niebauer J, Sallis R, Sawada SS, Sui X, Wisløff U; American Heart Association Physical Activity Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council on Cardiovascular and Stroke Nursing; Council on Functional Genomics and Translational Biology; Stroke Council. Circulation. 2016 Dec 13;134(24):e653-e699.*

The purpose of this statement is to review current knowledge related to the association between CRF and health outcomes, increase awareness of the added value of CRF to improve risk prediction, and suggest future directions in research. Although the statement is not intended to be a comprehensive review, critical references that address important advances in the field are highlighted. The underlying premise of this statement is that the addition of CRF for risk classification presents health professionals with unique opportunities to improve patient management and to encourage lifestyle-based strategies designed to reduce cardiovascular risk.

**AHA 2013: The importance of cardiorespiratory fitness in the United States: the need for a national registry: a policy statement from the American Heart Association.**

*Kaminsky LA, Arena R, Beckie TM, Brubaker PH, Church TS, Forman DE, Franklin BA, Gulati M, Lavie CJ, Myers J, Patel MJ, Piña IL, Weintraub WS, Williams MA; American Heart Association Advocacy Coordinating Committee, Council on Clinical Cardiology, and Council on Nutrition, Physical Activity and Metabolism. Circulation. 2013*

*Feb 5;127(5):652-62.*

The purpose of the present policy statement is to outline the importance of broadening the assessment of CRF and to provide the rationale for the development of a national adult CRF registry that would be representative of the entire US population. Additionally, this statement will outline how a national CRF database could enhance the value of CRF assessment in the US population and across environments, including the clinical setting and the workplace, as well as in the general public, to better inform our national policy efforts on PA, fitness, and health.

**EACPR/AHA 2012: Scientific Statement. Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations**

*Guazzi M, Adams V, Conraads V, Halle M, Mezzani A, Vanhees L, Arena R, Fletcher GF, Forman DE, Kitzman DW, Lavie CJ, Myers J; European Association for Cardiovascular Prevention & Rehabilitation; American Heart Association - Circulation. 2012 Oct 30;126(18):2261-74.*

CPX is well recognized as the gold standard aerobic Exercise Testing assessment. The use of CPX is well-established in the clinical setting for both patients with systolic HF, undergoing a pretransplant assessment, and individuals with unexplained exertional dyspnea. The evidence supporting the use of CPX in patients with confirmed or suspected PAH and secondary PH is also rapidly expanding and a strong case for the application of this Exercise Testing assessment in this population can now be made. There is also emerging evidence to demonstrate CPX elicits clinically valuable information in a number of other patient populations.

**AHA 2010: Clinician's Guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association**

*Balady GJ, Arena R, Sietsema K, Myers J, Coke L, Fletcher GF, Forman D, Franklin B, Guazzi M, Gulati M, Keteyian SJ, Lavie CJ, Macko R, Mancini D, Milani RV - Circulation. 2010 Jul 13;122(2):191-225.*

CPX (with ventilatory gas exchange measurements during exercise) offers the clinician the ability to obtain a wealth of information beyond standard exercise testing that, when appropriately applied and interpreted, can assist in the management of complex cardiovascular and pulmonary disease.

**EACPR 2009: Standards for the use of cardiopulmonary exercise testing for the functional evaluation of cardiac patients: a report from the Exercise Physiology Section of the European Association for Cardiovascular Prevention and Rehabilitation**

*Mezzani A, Agostoni P, Cohen-Solal A, Corrà U, Jegier A, Kouidi E, Mazic S, Meurin P, Piepoli M, Simon A, Laethem CV, Vanhees L - Eur J Cardiovasc Prev Rehabil. 2009 Jun;16(3):249-67.*

This study emphasizes the opportunities that CPET offers for the functional evaluation of cardiac patients, illustrating the wealth of information obtainable through an experienced use of this powerful tool. The choice of parameters to measure will depend on the specific goals of the functional evaluation in the individual patient, namely, exercise tolerance assessment, training prescription, treatment efficacy evaluation, investigation of exercise-induced adaptations of the O<sub>2</sub> transport/utilization system (whether of single links or the whole system), etc.

**AHA 2009: Recommendations for clinical exercise laboratories: a scientific statement from the American Heart Association**

*Myers J, Arena R, Franklin B, Pina I, Kraus WE, Balady GJ - Circulation. 2009 Jun 23;119(24):3144-61.*

The use of ventilatory expired gas analysis greatly improves both accuracy and reproducibility for assessing cardiopulmonary function compared with indirect estimation of oxygen uptake from work rate. In addition, the utilization of ventilatory expired gas analysis allows for the assessment of important submaximal cardiopulmonary responses, such as the ventilatory threshold,

**AHA 2007: Assessment of functional capacity in clinical and research settings: a scientific statement from the American Heart Association Committee on Exercise, Rehabilitation, and Prevention**

*Arena R, Myers J, Williams MA, Gulati M, Kligfield P, Balady GJ, Collins E, Fletcher G. - Circulation. 2007 Jul 17;116(3):329-43. Epub 2007 Jun 18.*

Ventilatory expired gas techniques during exercise testing have become more widely applied because they significantly increase the precision and yield of information from the exercise test. A shortcoming of standard exercise testing is the inherent inaccuracy in the estimation of exercise capacity from the work rate achieved on a treadmill or cycle ergometer.

**ACC/AHA 2002 guideline update for exercise testing**

*Gibbons RJ, Balady GJ, Bricker JT, Chaitman BR, Fletcher GF, Froelicher VF, Mark DB, McCallister BD, Mooss AN, O'Reilly MG, Winters WL, Gibbons RJ, Antman EM, Alpert JS, Faxon DP, Fuster V, Gregoratos G, Hiratzka LF,*

*Jacobs AK, Russell RO, Smith SC - J Am Coll Cardiol. 2002 Oct 16;40(8):1531-40.*

Measurement of expiratory gases during exercise testing can provide the best estimate of functional capacity, grade the severity of functional impairment, objectively evaluate the response to interventions that may affect exercise capacity, objectively track the progression of disease that may limit exercise capacity, and assist in differentiating cardiac from pulmonary limitations in exercise capacity.

## **CPET Prognostic Significance**

### **Cardiopulmonary Exercise Testing: What Is its Value?**

*Guazzi M, Bandera F, Ozemek C, Systrom D, Arena R. J Am Coll Cardiol. 2017 Sep 26;70(13):1618-1636.*

Cardiopulmonary exercise testing (CPET) provides a thorough assessment of exercise integrative physiology involving the pulmonary, cardiovascular, muscular, and cellular oxidative systems. Due to the prognostic ability of key variables, CPET applications in cardiology have grown impressively to include all forms of exercise intolerance, with a predominant focus on heart failure with reduced or with preserved ejection fraction.

### **A meta-analysis of the prognostic significance of cardiopulmonary exercise testing in patients with heart failure.**

*Cahalin LP, Chase P, Arena R, Myers J, Bensimhon D, Peberdy MA, Ashley E, West E, Forman DE, Pinkstaff S, Lavie CJ, Guazzi M - Heart Fail Rev. 2013 Jan;18(1):79-94.*

CPX is clearly an important component in the clinical assessment of patients with HF. The results of this meta-analysis strongly confirm this view and support a multivariate approach to CPX assessment. Specifically, the combined quantification of aerobic capacity (peak  $\dot{V}O_2$ ) and ventilatory efficiency (the  $\dot{V}E/\dot{V}CO_2$  slope and EO $\dot{V}$ ) appear to provide a more comprehensive insight into pathophysiology, disease severity, and prognosis.

### **Comprehensive use of cardiopulmonary exercise testing identifies adults with congenital heart disease at increased mortality risk in the medium term**

*Inuzuka R, Diller GP, Borgia F, Benson L, Tay EL, Alonso-Gonzalez R, Silva M, Charalambides M, Swan L, Dimopoulos K, Gatzoulis MA. Circulation. 2012 Jan 17;125(2):250-9.*

The combination of peak  $\dot{V}O_2$  and HRR as measured on CPX provides the greatest predictive information in addition to readily available clinical risk factors such as use of negative chronotropic agents, age, and low oxygen saturation in adults with CHD

### **Cardiopulmonary exercise testing in the clinical evaluation of patients with heart and lung disease**

*Arena R, Sietsema KE. - Circulation. 2011 Feb 15;123(6):668-80.*

The aerobic exercise assessment provides a wealth of clinically valuable information in patients with cardiac or pulmonary diseases. The addition of ventilatory and gas exchange measurements to the ECG and blood pressure monitoring used in conventional exercise tests provides more precise determination of aerobic capacity and unique insight into the independent and coupled functions of the cardiovascular, pulmonary, and skeletal muscle systems. Currently, the most widely used applications of CPX are the evaluation of patients diagnosed with systolic HF, preoperative assessment of selected patient populations, and diagnostic evaluation of patients with dyspnea.

### **The utility of cardiopulmonary exercise testing in the assessment of suspected microvascular ischemia**

*Chaudhry S, Arena R, Wasserman K, Hansen JE, Lewis GD, Myers J, Belardinelli R, LaBudde B, Menasco N, Boden WE. - Int J Cardiol. 2011 Apr 1;148(1):e7-9.*

Given the potential advantages of CPET to accurately detect and quantify reversible LV dysfunction in a non-invasive manner without radiation, utilization of this assessment technique in the evaluation and management of suspected microvascular ischemia may be clinically important. Incorporation of CPET may likewise be of diagnostic value to reduce the high rate of false positive stress ECG tests observed in women. Moreover, serial assessment with CPET enables a more accurate quantification of improvement in functional capacity (change in peak  $\dot{V}O_2$ ) and also enables the physician to discern the mechanism of improvement (improved peak stroke volume in this case).

### **The utility of cardiopulmonary exercise testing to detect and track early-stage ischemic heart disease**

*Chaudhry S, Arena RA, Hansen JE, Lewis GD, Myers JN, Sperling LS, LaBudde BD, Wasserman K - Mayo Clin Proc. 2010 Oct;85(10):928-32.*

in addition to identifying appropriate patients in need of escalating therapy for atherosclerosis, CPET was useful in monitoring progression and reversal of abnormalities of the coronary circulation in a safe and cost-effective manner without the use of radiation. Serial CPET parameters may be useful to track changes marking the progression and/or regression of the underlying global ischemic burden.

**ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult**  
*Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michl K, Oates JA, Rahko PS, Silver MA, Stevenson LW, Yancy CW, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B - Circulation. 2005 Sep 20;112(12):e154-235.*

Maximal exercise testing, with measurement of peak oxygen uptake, has been used to identify appropriate candidates for cardiac transplantation, to determine disability, and to assist in the formulation of an exercise prescription

#### **Applications of cardiopulmonary exercise testing in the management of cardiovascular and pulmonary disease**

*Myers J. - Int J Sports Med. 2005 Feb;26 Suppl 1:S49-55.*

A cardiopulmonary exercise test can supplement other clinical and exercise test information when precision is important, when the patient's symptoms are mixed, or when it is unclear why the patient was referred for exercise testing. Information from the test can also be used to support the important recommendation that the patient engage in an exercise program..

#### **Exercise-induced myocardial ischaemia detected by cardiopulmonary exercise testing**

*Belardinelli R, Lacalaprice F, Carle F, Minnucci A, Cianci G, Perna G, D'Eusanio G - Eur Heart J. 2003 Jul;24(14):1304-13.*

The addition of gas exchange analysis improves the diagnostic accuracy of standard ECG stress testing in identifying EIMI. A two-variable model based on O<sub>2</sub> pulse flattening duration and deltaVO<sub>2</sub>/deltawork rate slope had the highest predictive ability to identify EIMI.

### **CPET & Cardiac Rehabilitation**

#### **Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: a joint position statement of the EACPR, the AACPR, and the CACR**

*Mezzani A, Hamm LF, Jones AM, McBride PE, Moholdt T, Stone JA, Urhausen A, Williams MA - J Cardiopulm Rehabil Prev. 2012 Nov-Dec;32(6):327-50.*

The importance of functional evaluation through exercise testing prior to starting an aerobic training program is strongly emphasized, and an incremental cardiopulmonary exercise test, when available, is proposed as the gold standard for a physiologically comprehensive exercise intensity assessment and prescription.

#### **Secondary prevention through cardiac rehabilitation: physical activity counselling and exercise training: key components of the position paper from the Cardiac Rehabilitation Section of the EACPR**

*Corrà U, Piepoli MF, Carré F, Heuschmann P, Hoffmann U, Verschuren M, Halcox J; Document Reviewers, Giannuzzi P, Saner H, Wood D, Piepoli MF, Corrà U, Benzer W, Bjarnason-Wehrens B, Dendale P, Gaita D, McGee H, Mendes M, Niebauer J, Zwisler AD, Schmid JP - Eur Heart J. 2010 Aug;31(16):1967-74.*

A progressive increasing training regimen should be prescribed with regular follow-up controls (at least every 3–6 months), to adjust the duration and the level of the exercise to the reached level of tolerance. Peak oxygen consumption (Peak VO<sub>2</sub>) by cardiopulmonary exercise testing is the ideal physiologic marker of intensity

### **CPET & Pre-Operative Assessment**

#### **Cardiopulmonary Exercise Testing and Surgery.**

*Older PO, Levett DZH. Ann Am Thorac Soc. 2017 Jul;14(Supplement\_1):S74-S83*

Cardiopulmonary exercise testing provides an individualized estimate of patient risk that can be used to predict postoperative morbidity and mortality. This technology can therefore be used to inform collaborative decision-making and patient consent, to triage the patient to an appropriate perioperative care environment, to diagnose unexpected comorbidity, to optimize medical comorbidities preoperatively, and to direct individualized preoperative exercise programs.

#### **Cardiopulmonary exercise testing: a review of methods and applications in surgical patients.**

*Ridgway ZA, Howell SJ. Eur J Anaesthesiol. 2010 Oct;27(10):858-65.*

This review presents the physiological basis for CPX testing, methodology, advantages over other preoperative tests of cardiovascular function and guidance on the interpretation of CPX results in the perioperative setting.

### **Cardiopulmonary exercise testing: does it improve perioperative care and outcome?**

*Stringer W, Casaburi R, Older P. - Curr Opin Anaesthesiol. 2012 Apr;25(2):178-84*

Using a small number of important variables obtained from CPET, an accurate picture of the patient's future response to perioperative stress can be obtained. Consideration should be given to performing a CPET in any preoperative patient who has increased risk or is scheduled to undergo a high risk surgical intervention. This strategy assists the anesthetist, surgeon, patients, and their families in appropriate perioperative planning.

The CPET variables of peak oxygen uptake, anaerobic threshold, oxygen pulse, and ventilatory efficiency appropriately focus upon the cardiopulmonary reserve required to respond to metabolic stress and, therefore, are ideal to predict operative surgery outcomes. The focus should not be on using CPET to deny surgery to patients, but rather to define the level of postoperative care required to minimize risk.

### **Submaximal cardiopulmonary exercise testing predicts complications and hospital length of stay in patients undergoing major elective surgery**

*Snowden CP, Prentis JM, Anderson HL, Roberts DR, Randles D, Renton M, Manas DM. - Ann Surg. 2010 Mar;251(3):535-41.*

An objective measure of cardiorespiratory reserve was an independent predictor of a major surgical group with increased postoperative complications and hospital LOS. AT measurement significantly improved outcome prediction compared with an algorithm-based activity assessment.

### **Cardiopulmonary exercise testing: a review of methods and applications in surgical patients**

*Ridgway ZA, Howell SJ. - Eur J Anaesthesiol. 2010 Oct;27(10):858-65.*

Over the past decade, it has become an important preoperative assessment tool to evaluate functional capacity and predict outcomes in patients undergoing both cardiac and noncardiac surgery. A limited functional capacity as indicated by a low anaerobic threshold or  $VO_{2peak}$  has been shown to be associated with an increased incidence of perioperative complications in a number of surgical settings. Other reported variables, including the ventilatory equivalents for oxygen ( $VE/VO_2$ ) and carbon dioxide ( $VE/VCO_2$ ) and the millilitre of oxygen delivered per heartbeat or oxygen pulse [ $VO_2/\text{heart rate (HR)}$ ] may give indications as to the reasons for exercise limitation.

### **ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines**

*Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof EL, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Buller CE, Creager MA, Ettinger SM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Ornato JP, Page RL, Riegel B, Tarkington LG, Yancy CW. - J Am Coll Cardiol. 2007 Oct 23;50(17):1707-32.*

Functional status has been shown to be reliable for perioperative and long-term prediction of cardiac events.

### **Exercise anaerobic threshold and ventilatory efficiency identify heart failure patients for high risk of early death**

*Gitt AK, Wasserman K, Kilkowski C, Kleemann T, Kilkowski A, Bangert M, Schneider S, Schwarz A, Senges J. Circulation. 2002 Dec 10;106(24):3079-84.*

In addition to already-established prognostic values of cardiopulmonary exercise testing, our study demonstrates the high prognostic strength of  $VO_{2AT}$  for early and long-term mortality in CHF. The combination of  $VO_{2AT}$  and the VE versus  $VCO_2$  slope better identifies patients at risk for early death from CHF than peak  $VO_2$  who therefore should be considered as candidates for early heart transplantation.

### **Preoperative cardiopulmonary risk assessment by cardiopulmonary exercise testing**

*Older P, Smith R, Hall A, French C. - Crit Care Resusc. 2000 Sep;2(3):198-208.*

In patients who are about to undergo major intra-abdominal surgery, preoperative cardiopulmonary exercise testing is an excellent predictor of risk in the postoperative period. No other test is able to offer such a comprehensive preoperative risk evaluation for an operative patient.

### **Cardiopulmonary exercise testing as a screening test for perioperative management of major surgery in the elderly**

*Older P, Hall A, Hader R. - Chest. 1999 Aug;116(2):355-62.*

The results of CPX have a very high predictive value for patients at risk of death from cardiopulmonary causes in the postoperative period. It is even more reliable at detecting those not at risk, in that there were no deaths related to cardiopulmonary complications in any patient we identified through CPX testing as fit for major surgery with ward management.

## Safety Issues

**Supervision of exercise testing by nonphysicians: a scientific statement from the American Heart Association.**

*Myers J, Forman DE, Balady GJ, Franklin BA, Nelson-Worel J, Martin BJ, Herbert WG, Guazzi M, Arena R. Circulation. 2014 Sep 16;130(12):1014-27.*

In most cases, clinical exercise tests can be safely supervised by properly trained nonphysician health professionals if the individual supervising the test meets competency requirements for exercise test supervision, is fully trained in cardiopulmonary resuscitation, and is supported by a physician skilled in exercise testing or emergency medicine who is in close proximity for pretest assessments or complications that may arise.

**The safety of cardiopulmonary exercise testing in a population with high-risk cardiovascular diseases.**

*Skalski J, Allison TG, Miller TD. Circulation. 2012 Nov 20;126(21):2465-72.*

The major value of this article is the demonstration that CPX is a reasonably safe procedure in a population of patients with a spectrum of established cardiovascular diseases, many of which represent high-risk conditions and are considered relative contraindications to stress testing.<sup>1</sup> It is important to recognize that all of the patients in this study had their cardiovascular diagnoses established before CPX, and that testing was carefully performed in an experienced laboratory at a tertiary care center. There are subsets of patients with the most extreme variants of these conditions, in whom stress testing represents an absolute contraindication, such as a patient with severe symptomatic aortic stenosis. However, for other patients with these disorders, CPX appears to be reasonably safe and can serve as a helpful aid in the management of these patients