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STATEMENT

Summary Statement on Cardiopulmonary Exercise Testing in Chronic Heart Failure due to Left Ventricular Dysfunction Recommendations for Performance and Interpretation

Documento ufficiale sull'utilizzo del test ergometrico cardiopolmonare nello scompenso cardiaco dovuto a disfunzione ventricolare sinistra Raccomandazioni per l'esecuzione e l'interpretazione

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ABSTRACT: ***Summary Statement on Cardiopulmonary Exercise Testing in Chronic Heart Failure due to Left Ventricular Dysfunction. Recommendations for Performance and Interpretation. U. Corrà, M.F. Piepoli.***

Cardiopulmonary exercise testing (CPET) is a non-invasive tool that provides the physician with relevant information to assess the integrated response to exercise involving pulmonary, cardiovascular, haematopoietic, neuro-psychological, and skeletal muscle systems. Measurement of expiratory gases during exercise allows the best estimate of functional capacity, grade the severity of the impairment, objectively evaluate the response to interventions, objectively track the progression of disease, and assist in differentiating cardiac from pulmonary limitations in exercise tolerance. To achieve optimal use of this test in every day clinical practice, clarification of conceptual issues and standardization of CPET practices are necessary. Recently, a Statement on Cardiopulmonary Exercise Testing in Chronic Heart Failure due to Left Ventricular Dysfunction, by the Gruppo Italiano di Cardiologia Riabilitativa and endorsed by the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology, has been published. Here are resumed the cardinal points of the Statement: (1) Definition of Cardiopulmonary Exercise Testing Parameters for Appropriate Use in Chronic Heart Failure, (2) How to Perform Cardiopulmonary Exercise Testing in Chronic Heart Failure, (3) Interpretation of Cardiopulmonary Exercise Testing in Chronic Heart Failure and Future Applications.

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Introduction

Cardiopulmonary exercise testing (CPET) is a non-invasive tool that provides the physician with relevant information for clinical decision making [1-4]. It globally assesses the integrated response to exercise involving the pulmonary, cardiovascular, haematopoietic, neuro-psychological, and skeletal muscle systems. Measurement of expiratory gases during exercise allows the best estimate of functional capacity, grade the severity of the impairment, objectively evaluate the response to interventions, objectively track the progression of disease, and assist in differentiating cardiac from pulmonary limitations in exercise tolerance.

Recently an increasing use of CPET has been fuelled by several factors:

i) scientific advances in exercise physiology and increased awareness of the importance of the integrated exercise response in clinical assessment;
ii) data derived from CPET have proved to be reliable and important measures in the evaluation and management of chronic heart failure (CHF) patients with the understanding that resting pulmonary and cardiac function testing cannot reli-

ably predict exercise performance and functional capacity;

iii) overall health status and prognosis are predicted better by indices of exercise tolerance than by resting measurements;

iv) CPET provides reproducible indices of exercise limitation, cardiac and pulmonary function and as such it offers a useful means for both risk stratification and indication of the most appropriate therapeutic approaches;

v) advances in technology including the development of automated exercise systems with enhanced data acquisition and management and subject- monitoring capabilities.

To achieve optimal use of this test in every day clinical practice, clarification of conceptual issues and standardization of CPET practices are necessary. Recently, a Statement on Cardiopulmonary Exercise Testing in Chronic Heart Failure (CHF) due to Left Ventricular Dysfunction, by the Gruppo Italiano di Cardiologia Riabilitativa (GICR) and endorsed by the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology, has been published in the European Journal of Cardiovascular Prevention and Rehabilitation (EJCPR). The document is accessible in the April, June and August issues of 2006 [5-7].

The committee consisted of acknowledged experts in CPET, as well as general cardiologists: all contributors had a broad range of clinical and research expertise and conceptual approaches to the topic, and both the academic and private practice sectors were represented. The Statement was reviewed by two outside reviewers, nominated by the EJCPR editors, and, as a final point, and importantly, all three sections were written within the last 6 months of 2005, and therefore information will remain clinically relevant for some time.

Purpose, scope and audience

This exhaustive and collaborative work intended to produce a comprehensive, practical, timely, conceptually balanced document on the use of CPET in patients with CHF due to left ventricular dysfunction, and consisted of recommendations on the interpretation, standardization of performance and clinical application of CPET in CHF based on contemporary scientific knowledge and technical advances. Recommendations were based on best available evidence, current prevailing scientific knowledge, and expert opinion, attempting to identify areas of controversy and to note clearly those areas where recommendations do not achieve clear consensus, and where alternative approaches are possible.

The intended audience includes those who perform clinical CPET, and those who use the results of CPET to assist in clinical decision-making and in the prescription of exercise training programmes. Nonetheless, this comprehensive update will be particularly useful to clinical readers challenged with keeping up with the remarkable information expansion in the area of CPET and the on-going need to assess clinical relevancy.

The document is available in 3 sections: (1) Definition of Cardiopulmonary Exercise Testing Parameters for Appropriate Use in Chronic Heart Failure, (2) How to Perform Cardiopulmonary Exercise Testing in Chronic Heart Failure, (3) Interpretation of Cardiopulmonary Exercise Testing in Chronic Heart Failure and Future Applications. Tables 1-3 present the primary contents of the statements.

First section, *"Definition of Cardiopulmonary Exercise Testing Parameters for Appropriate Use in Chronic Heart Failure"*

The clinical utility, strengths, and limitations for all individual CPET measurements, including the reproducibility of variables have been discussed in detail (table 1). Gas exchange and ventilatory measurements have been analysed considering their clinical application and interpretation in CHF with normal subjects as references, and for all individual parameters proved clinical application and pitfalls have been described and judged.

An impressive number of variables is typically measured or derived during CPET, and the utility of many of these measurements is well known, while for other, their clinical usefulness is yet not settled. Oxygen uptake (VO_2), anaerobic ventilatory threshold (AT) and ventilatory response to exercise (VE/VCO_2 slope) have been extensively analyzed. As regards VO_2 peak, beside pathophysiological expressions and phases in CHF, normalization, exercise mode and protocol, and data sampling, that may potentially and substantially vary a given VO_2peak value, have all been contemplated for interpretation intent. Concerning AT, although mechanisms, clinical applications, and mode of AT measurements have been insightfully discussed, the "statements message" is that accuracy of the AT determined by noninvasive methods can be influenced by physician's knowledge and familiarity, protocol adopted, system utilized, data collection and sampling, subjects studied (i.e. severity of disease and co-

Table 1. - Contents of the first section: **"Definition of Cardiopulmonary Exercise Testing Parameters for Appropriate Use in Chronic Heart Failure"**

Oxygen Uptake (VO_2)

VO_2 - Work Rate Relationship ($\Delta VO_2/\Delta WR$)

Definition VO_{2max} - VO_{2peak}

Kinetics of VO_2 recovery after exercise

CO_2 Output (VCO_2)

Peak Respiratory Exchange Ratio (VCO_2/VO_2)

Anaerobic Threshold (AT)
1. Mechanisms
2. Clinical applications
3. Measurements

Ventilation
1. Pulmonary diffusion capacity
2. Pulmonary perfusion
3. Dead space ventilation
4. VE/VCO_2 slope

Cardiac Output
1. Heart rate (HR)
2. HR - VO_2 relationship
3. Oxygen pulse (VO_2/HR)

Blood Pressure Response

Table 2. - Contents of the second section: **"How to Perform Cardiopulmonary Exercise Testing in Chronic Heart Failure"**

SAFETY: RISK AND CONTRAINDICATIONS	
1. Environmental conditions	
2. Personnel	
3. Patient preparation and information	
EQUIPMENT	
1. Collection of expired ventilation	
2. Flow sensing devices	Pressure-differential devices, pneumotachometers
	Modern electronic turbines
	Pitot tube
4. Mass flow sensors (hot wire anemometer)	
3. Gas analysers	Mass spectrometer
	Oxygen analysers
	Carbon dioxide analyser
4. Metabolic measurement techniques	Bag collection
	Mixing chamber
	Breath-by-breath method
5. Gas exchange measurements and calculations	
6. Calibration procedures and quality control	
EXERCISE PROTOCOLS	
1. Generic types of protocols	
2. Specific exercise protocols	Treadmill exercise
	Cycle ergometer
MODALITY OF PERFORMANCE: HOW TO CONDUCT THE TEST	
1. Personnel	
2. Confirmation of patient candidacy for CPET	
3. Exercise modality	
4. Data Monitoring	
DATA REPORTING	

Table 3. - Contents of the third section: **"Interpretation of Cardiopulmonary Exercise Testing in Chronic Heart Failure and Future Applications"**

INTERPRETATION
1. Pharmachological therapy efficacy evaluation
   - Effects of heart failure therapy on CPET parameters
2. Non-Pharmachological therapy efficacy evaluation
   - Cardiac resynchronization therapy (CRT)
   - Exercise rehabilitation prescription and evaluation
3. Prognostic evaluation

SPECIFIC APPLICATIONS AND FUTURE PROSPECTIVES
1. Female
2. Elderly population
3. Valvular heart diseases
   - Aortic Stenosis
   - Aortic Regurgitation
   - Mitral Stenosis
   - Mitral Regurgitation
4. Hypertrophic cardiomyopathy

morbidities), and peculiarities and variances of the methods used. Finally, the pathophysiology determining exercise ventilatory inefficiency in CHF has been argued, while its clinical and prognostic implications have been discussed in the 3th section. Overstated VE/VCO_2 slope and periodic breathing on exertion are recognized markers of abnormal breathing control: the complex and not entirely known core mechanicistic hypothesis involves reflex abnormalities, central and peripheral neurogenic and humoral response from peripheral (carotid) and central chemoreceptors, ergoreceptors, metaboreceptors, the role of muscle deconditioning and metabolic toxicity, reduced cardiac output, circulatory delay and hemodynamic fluctuations, and high functional dead space and tidal volume ratio. Ventilatory, metabolic and hemodynamic hypotheses have been proposed in this section.

Second section, *"How to Perform Cardiopulmonary Exercise Testing in Chronic Heart Failure"*

Basic and practical information related to safety, equipment, methodology, exercise protocols, conduct of the test and quality control issues for CPET have been addressed (table 2). Indications, absolute and relative contraindications should be carefully considered by reference to medical history and physical examination (table 4 and 5) [6]. Although symptom-limited CPET is a relatively safe procedure, bedside patient clinical circumstances and evaluation, environmental conditions and personnel attitudes and excellence are imperative safety features. The laboratory in which the CPET is carried out should have room enough for all the required equipment plus allow easy patient access in the case of emergency. The resuscitation and exercise equipment must be arranged so as to facilitate cardiopulmonary resuscitation in the

Table 4. General indications for cardiopulmonary exercise testing

Evaluation of exercise tolerance
Evaluation of undiagnosed exercise intolerance
Evaluation of patients with cardiovascular disease
- Functional evaluation and prognosis
- Selection for cardiac transplantation
- Exercise prescription
- Monitoring response to exercise training

Evaluation of patients with respiratory disease
- Functional impairment assessment
- Specific respiratory disease evaluation.
- Exercise evaluation and prescription for pulmonary rehabilitation

Specific clinical applications
- Preoperative evaluation
- Clinical relevant research purpose
- Evaluation for impairment-disability
- Evaluation for lung, heart-lung transplantation

Table 5. - Contraindications to exercise testing

Absolute
- Acute myocardial infarction
- High-risk unstable angina
- Uncontrolled cardiac arrhythmias causing symptoms or hemodynamic compromise
- Symptomatic severe aortic stenosis.
- Uncontrolled symptomatic heart failure
- Acute pulmonary embolus or pulmonary infarction
- Acute myocarditis or pericarditis
- Acute aortic dissection
- Severe orthopedic limitation
- Inability to provide informed consent

Relative *(can be superseded, if benefits of exercise outweigh the risks)*
- Left main coronary stenosis
- Moderate stenotic valvular heart disease
- Electrolyte abnormalities
- Severe arterial hypertension
- Tachyarrhythmias or bradyarrhythmias
- Hypertrophic cardiomyopathy and other forms of outflow tract obstruction
- Mental or physical impairment leading to inability to exercise adequately
- High-degree atrioventricular block

space immediately adjacent to the exercise equipment. All clinical exercise stress laboratories should be equipped with some type of alarm so that the help of nearby personnel can be summoned speedily. Concerning personnel, clinical laboratory should be under the direction of a cardiologist certified in advanced cardiovascular life support, with expert knowledge of exercise physiology and with training in calibration, quality control, performance and interpretation of cardiopulmonary exercise testing. Continuing competence in CPET requires regular, continued performance: performance of only a rare test can lead to missed or inappropriate interpretation. Beside physicians, staff may include properly trained nurse, exercise physiologists, physical therapists or specialized medical technicians. The number of persons present in the laboratory is determined by measurements to be carried out (assessment of invasive parameters in exercise) and by the patient's clinical condition. Table 6 provides a list of the necessary equipment and personnel for a CPET laboratory.

The proper interpretation of CPET data depends on accurate data collection and correct calculation: consequently, an adequate knowledge of equipment, the mode of test conduction are fundamental pre-requisite for optimal clinical utilisation of CPET. CPET users have the responsibility for assuring that mea-

Table 6. - Ergospirometry laboratory: equipment and personnel

General environment
1. Laboratory should be broad enough for all the required equipment and allow easy patient access in the case of emergency
2. Well illuminated, with temperature and humidity control
3. Barometer station with thermometer and hygrometer is required
4. Table for evaluating the perceived effort clearly visible

Exercise equipment
1. 12-leads electrocardiogramm
2. Electrocardiographic monitor
3. Sphygmomanometer
4. Treadmill or cycle ergometer
5. Blood pressure measurement
6. Pulse-oximetry

Gas exchange measurement
1. Volume/flow devices: volume measurement and flow measurement
2. Gas analysers or mass spectrometer
3. Disposable materials (mouthpieces, masks, saliva traps, collecting tubes, cleaning stuff)
4. Calibration materials (large-volume syringe, tubes)

Resuscitation equipment

Personnel

Number limited to those needed for making measurement and for patients safety: physician / cardiologist, and nurse surements remain accurate. Although a deeply description of CPET manufacturing equipment is beyond the scope of the statement, basic and necessary technical properties, critical characteristics and hazards of flow sensing devices, gas analysers and metabolic measurement techniques have been offered to help CPET users in daily performance. CPET, especially when it features breath-by-breath gas exchange analysis, requires meticulous attention to calibration procedures to assure accurate and reproducible measurements. Since the two main causes of errors in CPX results are errors in calibration and leaks, a good practice is to calibrate the system daily.

Patient collaboration and exercise protocol selection are essential to optimize the clinical-diagnostic value of CPET. Usually, if patients are adequately informed and instructed they will perform the maximum effort possible in relation to their condition, thus providing adequate information and enabling a reliable interpretation of the test. For this reason, the patient should be carefully prepared (table 7). Complete spirometry assessment with determination of the maximum voluntary ventilation (MVV), blood gas analysis at rest, in the case of suspected hypoxemia, blood cell count, and knowledge of the pharmacological treatment can support CPET interpretation. Information on the patient's habitual level of physical activity will help in choosing the most appropriate exercise protocol.

Finally, having performed the test appropriately, the investigator then needs to format the results in a manner that optimizes the ability to discriminate essential response features; i.e. to establish "interpretive clusters" of the variables of interest. An example of Cardiopulmonary Summary Exercise Test Data Report has been provided, defining the most important information that should be incorporated in the final report (table 8).

Table 7. - Pre-test information: what should be known before CPET

Specific question being addressed by CPET

General information

Age, actual height and weight, level of physical activity and occupational history. Smoking habits. Type of exercise limitation. Previous or recent cardiovascular evaluations

Pertinent pre-test clinical findings

Diagnosis. Physical examination. Resting electrocardiogram. Medications
Establish the presence of contraindications to CPET
Optional: chest roentgenograms, resting spirometry, arterial blood gas analysis at rest. Blood cell count: hemoglobin

Equipment familiarization and registration

1. Provide general advice on the modality of exercise
2. Provide general advice on exercise protocol
3. Seat height adjustment for cycle ergometer
4. Provide advice for moving off the treadmill belt with confidence
5. Twelve lead ECG continuous monitoring
6. Non invasive blood pressure monitoring
7. Define a non-verbal transmit strategies for describing symptoms and CPET interruption criteria
8. Try mask or mouthpiece and nose clip before
9. Expiratory gases monitoring

Table 8. - Report of cardiopulmonary exercise testing (CPET): what should be included

Pre-test information

1. Specific question being addressed by CPET
2. General information.
3. Clinical information: diagnosis, medications, resting electrocardiogram, blood pressure

Information about exercise modality and equipment

1. Modality of exercise
2. Exercise protocol
3. Modality of gas sampling

Observations during exercise testing

1. Reason(s) for stopping exercise
2. Complication occurrence
3. Subjective assessment of effort
4. Gas exchange and ventilatory data at peak and at ventilatory anaerobic threshold (if determined): absolute value and percentage relative to reference
5. Description of heart rate response and ECG changes
6. Blood pressure response

Exercise test interpretation

1. Presence and severity of functional impairment
2. Define the plausible reason for functional impairment
3. Provide a comparison with previous functional evaluation (if available)

Third section, *"Interpretation of Cardiopulmonary Exercise Testing in Chronic Heart Failure and Future Applications"*

Interest has been focused on a reliable and integrative interpretation of CPET. Optimal use of CPET in clinical practice requires appropriate data presentation and a flexible interpretative strategy. The greatest potential impact on decision-making process may rest not as much on the utility of any individual measurement, although some are obviously more important than other, but rather on the integrative use. Such integrative approach relies on interrelationship, trending phenomena, and patterns of key gas exchange variable responses. An integrative, multiparametric approach has been discussed in different clinical applications for exercise prescription and monitoring, functional evaluation of drug therapy or cardiac resynchronization therapy efficacy, and risk stratification.

Serial assessment of exercise capacity poses greater challenges than the single determination, introducing both methodological and clinical issues. In this context, test reproducibility is fundamental, and VO_2peak is generally considered reproducible. Beside changes in the underlying disease process(es) and in medication, factors that may contribute to the variability in CPET measurements during serial evaluations include patient motivation and instructions/inducement, the time of day, testing procedure, equipment/calibration errors. Thus, to improve reproducibility, serial testing should be performed at the same time of the day: background therapy should be taken in the same doses and time intervals before each exercise testing. Every clinical exercise laboratory should provide short- and long-term coefficients of variation of peak and submaximal gas exchange parameters, and changes over time of gas exchange measurements should be interpreted against inter-test coefficients of variation. A variation of peak gas exchange variables within the variability range should be considered potentially neutral. Changes over time of gas exchange parameters should be expressed as a percentage of baseline capacity, in order to avoid under- and over-estimation with absolute values. An increase of 2 ml/kg/min of VO_2peak may represent on the one hand a fairly modest gain for patients with VO_2peak of 20 ml/kg/min. (+10%), but on the other a consistent improvement for patients with VO_2peak of 10 ml/kg/min (+20%). Moreover, as stated before, time-related changes of gas exchange parameters over time should be interpreted according to variability of measurement range: if coefficient of variation of VO_2peak is 4%, we may assume that change VO_2peak between –4% and +4% may be related to measurement variability, above 4% it is more likely to be a real improvement, below 4% a warning of decline. Examples are reported in table 9.

With reference to risk discrimination, since peak VO_2 is one of the most potent prognostic variables ever discovered and almost all patient management decisions are driven by the clinician's assessment of the patient's prognosis, CPET has crucial role in clinical practice in CHF. At the side of peak VO_2, several CPET indices have been proposed to improve outcome prediction: although each single exertional parameter awards additional outcome discrimination, with the appeal of providing, for clinicians, a convenient "high risk/low risk" categorization, such a dichotomous approach that forces patients into one of two categories tends to oversimplify the issue and is of limited relevance in patients with CHF, which is a complex, heterogeneous clinical condition. Moreover, only few CEPT parameters have been widely recognized and translated in clinical reality. Thus, it seems more useful to substantiate complementary role of CPET parameters implementing an integrative, multiparametric approach.

Finally, future indication of CPET will be addressed, suggesting and promoting an extended candidacy either to all CHF patients, including those at high risk or most vulnerable, such as female, elderly, and patients with implantable cardioverter defibrillator (ICD) or to every clinical setting where objectively definition of exercise capacity provides implications for medical, surgical, and social decision making.

Conclusions

Gas exchange analysis is an imperfect science and considerable errors can occur if specific procedures are not followed to minimize them. Thus, although an appropriate *modus-operandi* adds cost and time to the test, it is a fundamental pre-requisite for proficient and optimal clinical use. Both appropriateness and uniformity of performance and interpretation enhance the critical role of CPET as risk estimation tool and gatekeeper of transplantation listing. Moreover, gas exchange measurements during exercise impacts and enhances the clinical decision-making process in CHF, providing an accurate assessment of severity, progression of disease and

Table 9. - Exercise Tolerance as a Guide to Clinical Management of Chronic Heart Failure. The proposal for an individual approach

	Patient n. 1	**Patient n. 2**
Peak VO_2 (ml/kg/m.) at baseline evaluation	10	20
Laboratory peak VO_2 variability - *Coefficient of variation*	4%	4%
Changes in peak VO_2 (ml/kg/m) related to measurement variability	0.4	0.8
Within peak VO_2 variability (ml/kg/m.)	9.6-10.4	19.2-20.8
Therapeutic efficacy (ml/kg/m.)	> 10.4	> 20.8
Warning decrease in peak VO_2 (ml/kg/m.)	< 9.6	< 19.2

response to therapy. Since CPET use is still very limited because it is traditionally considered a complex methodology requiring a high level of organization and skilled processes, the authors are confident that a more evidenced-based approach to the interpretation of CPET, as described in the Statement, will stimulate either a further widespread use of CPET in the management of CHF patients, and an implementation of CPET in cardiac rehabilitation and prevention.

Riassunto

Il test ergometrico cardiopolmonare (TECP) è uno strumento non invasivo utile nella valutazione della risposta integrata all'esercizio coinvolgente il sistema polmonare, cardiaco, ematopoietico, neuropsicologico e del muscolo scheletrico. La misurazione dei gas espiratori durante esercizio fornisce una migliore stima della capacità funzionale, del grado di severità della limitazione funzionale, una valutazione oggettiva della risposta agli interventi, una traccia oggettiva della progressione della malattia, e aiuta a differenziare una ridotta tolleranza all'esercizio di origine cardiaca da quella polmonare. Per ottenere un utilizzo ottimale di questo test nella pratica clinica, è necessario un chiarimento circa i contenuti e la standardizzazione della esecuzione del TECP. Recentemente, il Gruppo Italiano di Cardiologia Riabilitativa, congiuntamente al "Working Group on Cardiac Rehabilitation and Exercise Physiology" della Società Europea di Cardiologia, ha pubblicato un documento ufficiale sull'utilizzo del test ergometrico cardiopolmonare nello scompenso cardiaco dovuto a disfunzione ventricolare sinistra. Vengono qui riassunti i punti chiave di questo documento: (1) definizione dei parametri del test cardiopolmonare per un appropriato utilizzo nello scompenso cardiaco, (2) modalità di esecuzione di un test ergometrico cardiopolmonare nello scompenso cardiaco, (3) interpretazione del test ergometrico cardiopolmonare nello scompenso cardiaco e future applicazioni.

References

1. American Thoracic Society; American College of Chest Physicians. ATS/ACCP Statement on cardiopulmonary exercise testing. *Am J Respir Crit Care Med* 2003; 167: 211-277.
2. Wasserman K, Hansen JE, Sue DY, Whipp BJ, Casaburi R. Principles of exercise testing and interpretation: including pathophysiology and clinical applications, 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1999.
3. Weisman IM, Zeballos RJ. Cardiopulmonary exercise testing: the need for standardization. *Pulm Perspect* 1992; 9: 5-8.
4. Costanzo MR, Augustine S, Bourge R, Bristow M, O'Connell JB, Driscoll D, Rose E. Selection and treatment of candidates for heart transplantation. A statement for health professionals from the Committee on Heart Failure and Cardiac Transplantation of the Council on Clinical Cardiology, American Heart Association. *Circulation* 1995; 92: 3593-3612.
5. Task Force of the Italian Working Group on Cardiac Rehabilitation Prevention; Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology; Piepoli MF, Corrà U, Agostoni PG, Belardinelli R, Cohen-Solal A, Hambrecht R, Vanhees L. Statement on cardiopulmonary exercise testing in chronic heart failure due to left ventricular dysfunction: recommendations for performance and interpretation**.** ***Part I: Definition of cardiopulmonary exercise testing parameters for appropriate use in chronic heart failure.*** *Eur J Cardiovasc Prev Rehabil* 2006;13: 150-164.
6. Task Force of the Italian Working Group on Cardiac Rehabilitation Prevention; Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology; Piepoli MF, Corrà U, Agostoni PG, Belardinelli R, Cohen-Solal A, Hambrecht R, Vanhees L. Statement on cardiopulmonary exercise testing in chronic heart failure due to left ventricular dysfunction: recommendations for performance and interpretation. ***Part II: How to Perform Cardiopulmonary Exercise Testing in Chronic Heart Failure.*** *Eur J Cardiovasc Prev Rehabil* 2006; 13: 300-311.
7. Task Force of the Italian Working Group on Cardiac Rehabilitation Prevention; Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology; Piepoli MF, Corrà U, Agostoni PG, Belardinelli R, Cohen-Solal A, Hambrecht R, Vanhees L. Statement on cardiopulmonary exercise testing in chronic heart failure due to left ventricular dysfunction: recommendations for performance and interpretation**.** ***Part III: Interpretation of Cardiopulmonary Exercise Testing in Chronic Heart Failure and Future Applications.*** *Eur J Cardiovasc Prev Rehabil* 2006; 13: 485-494.

Appendix

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