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French Society of Cardiology guidelines on exercise tests (part 1): Methods and interpretation

Société française de cardiologie recommandations pour les épreuves d'effort (partie 1) : méthodes et interprétation

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Abbreviations: BP, blood pressure; CAD, coronary artery disease; CPET, cardiopulmonary exercise test; ET, exercise test; HR, heart rate; MET, metabolic equivalent of the task; MHR, maximal heart rate; SpO₂, oxygen saturation; VCO₂, carbon dioxide output; VE, volume of expired gas; VO₂, oxygen uptake; VT, ventilatory threshold.

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KEYWORDS

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Summary The exercise test is still a key examination in cardiology, used for the diagnosis of myocardial ischemia, as well as for the clinical evaluation of other heart diseases. The cardiopulmonary exercise test can further define functional capacity and prognosis for any given cardiac pathology. These new guidelines focus on methods, interpretation and indications for an exercise test or cardiopulmonary exercise test, as summarized below. The safety rules associated with the exercise test must be strictly observed. Interpretation of exercise tests and cardiopulmonary exercise tests must be multivariable. Functional capacity is a strong predictor of all-cause mortality and cardiovascular events. Chest pain, ST-segment changes and an abnormal ST/heart rate index constitute the first findings in favor of myocardial ischemia, mostly related to significant coronary artery disease. Chronotropic incompetence, abnormal heart rate recovery, QRS changes (such as enlargement or axial deviations) and the use of scores (based on the presence of various risk factors) must also be considered in exercise test interpretation for a coronary artery disease diagnosis. Arrhythmias or conduction disorders arising during the exercise test must be considered in the assessment of prognosis, in addition to a decrease or low increase in blood pressure during the exercise phase. When performing a cardiopulmonary exercise test, peak oxygen uptake and the volume of expired gas/carbon dioxide output slope are the two main variables used to evaluate prognosis.

MOTS CLÉS

Recommandations
françaises ;
Épreuve d'effort ;
Test
cardiopulmonaire ;
Sécurité ;
Interprétation

Résumé L'épreuve d'effort (EE) reste un examen clé en cardiologie pour le diagnostic de l'ischémie myocardique et pour l'évaluation clinique des autres cardiopathies. Le test cardiopulmonaire (CPT) basé sur l'analyse de la mesure des gaz expirés peut préciser la capacité fonctionnelle individuelle et estimer le pronostic des cardiopathies. Ces recommandations, résumées ci-dessous, font le point sur la méthodologie, l'interprétation et les indications de ces deux tests. Les règles de sécurité doivent être strictement respectées. L'interprétation de l'EE et du CPT doit être multivariée. La capacité fonctionnelle est un puissant facteur prédictif de la mortalité toutes causes et des événements cardiovasculaires. La douleur thoracique, les anomalies du segment ST et de l'index ST/fréquence cardiaque sont les premiers signes en faveur d'une ischémie myocardique le plus souvent en rapport avec des lésions coronaires. L'insuffisance chronotrope, une fréquence de récupération anormale, des modifications des QRS (élargissement, déviation axiale) et l'utilisation de score (basés sur la présence de différents facteurs de risque) doivent aussi être pris en considération pour le diagnostic de la maladie coronaire. Les troubles du rythme et de la conduction survenant pendant l'examen sont considérés comme des facteurs pronostiques comme la diminution ou une augmentation insuffisante de la pression artérielle pendant l'exercice. Lors de l'analyse des gaz expirés, le pic de consommation d'oxygène, la pente du rapport ventilation par la production de gaz carbonique sont les deux principaux paramètres pronostiques utilisés.

Background

Given that the current French guidelines date from 1997, the Groupe Exercice Readaptation et Sport (GERS; Exercise Rehabilitation and Sport Group) of the French Society of Cardiology has decided to publish new guidelines, taking into account the various works that have been published over the past decades [1,2]. Here, part 1 of these new guidelines provides an overview of the safety conditions and methodology required to perform and interpret an exercise test (ET) or a cardiopulmonary ET (CPET), which consists of an ET coupled with expired gas analysis; part 2 focuses on the extended indications for ETs and CPETs in cardiology.

Risks and safety

An ET is associated with a risk of fatal adverse events that is estimated to be <0.01%, and a risk of an event requiring medical intervention of <0.2% [3]. Hence, strict observation of contraindications and criteria for termination is necessary (Tables 1 and 2).

The ET laboratory must either comprise an intensive cardiac care unit or have the facility to allow rapid patient transfer to an intensive cardiac care unit in a different medical center. In the latter case, the affiliated emergency room must be equipped with the material required for cardiac resuscitation to be performed while awaiting patient transfer.

The ET laboratory must contain: a telephone to summon assistance; a source of oxygen; a ready-to-use aspiration system; ergometers; a 12-lead exercise electrocardiogram machine with permanent electrocardiogram monitoring (at least three simultaneous leads); a blood pressure (BP) measuring device; and a crash cart with a defibrillator [4]. It is also recommended, but not mandatory, to include an oximeter and a CPET device in the ET laboratory.

Before the ET, the patient must receive verbal information, particularly regarding the benefits, risks and possible alternatives to the examination, in addition to written information on the consent form, which should be signed and included in the patient's chart (refer to the model proposed on the French Society of Cardiology's website (<https://www.sfcadio.fr>), in accordance with article L1111-2 of the Public Health Code).

The ET must be conducted under the supervision of a cardiologist. During an ET or CPET, the laboratory must have the means to provide immediate cardiac resuscitation measures performed by the cardiologist, with the help of a qualified assistant (technician, paramedic or physician), trained regularly in ET, CPET and emergency care (attestation of emergency care level 1 training).

Methodology

The ET consists of maximal or symptom-limited exercise, with continuous recording of an electrocardiogram, BP and other clinical variables.

Patient preparation

The patient must not eat for a couple of hours before the ET. The skin must be well prepared to optimize electrocardiogram signals. Precordial leads are placed in the traditional manner; it is recommended that peripheral leads are placed on the iliac crests and subclavicular regions [2].

Analysis of expired gases

A CPET with continuous monitoring of oxygen saturation (SpO_2) allows evaluation of the respiratory, cardiovascular and muscular responses that occur during exercise [5–7].

Exercise protocol

The protocol is individualized according to the patient's maximal predicted capacity, corrected by the level of estimated physical activity [6–8].

The exercise protocol is based on a gradual workload increase after a warm-up period. An effort that progresses too rapidly will overestimate the patient's physical capacity. Inversely, the physical capacity will be underestimated if the effort progresses too slowly [6]. An ergometer ramp test protocol is recommended for CPET assessment, with the workload being increased continuously.

Criteria for termination of ET

The ET must be stopped when the patient reaches exhaustion or when symptoms or electrocardiogram findings requiring exercise cessation arise or at the patient's request (Table 2) [2]. The ET is maximal when at least one criterion listed in Table 3 is present [9]. Reaching the predicted maximal heart rate (MHR) does not constitute a criterion for ET termination.

Recovery

The recovery period must be prolonged until any abnormal clinical or electrocardiogram finding returns to baseline (requiring at least 3–6 minutes) [2]. Passive recovery can be recommended, as it is usually well-tolerated and permits a more accurate diagnosis of coronary artery disease (CAD) by increasing examination sensitivity, as well as allowing the use of recovery heart rate (HR) as a prognostic criterion [10].

Functional capacity

The maximal work performed is expressed by the power in watts on the bicycle or the slope and speed on the treadmill or the exercise duration. Oxygen uptake (VO_2) is expressed in L/min, mL/min/kg or metabolic equivalent of the task (MET) (1 MET = 3.5 mL oxygen per kilogram of body weight per minute [mL/min/kg]) [7]. The value obtained must be compared with the predicted value [11]. The double product (maximal systolic BP \times MHR) evaluates the myocardial workload.

Table 1 Contraindications [2].**Absolute contraindications**

- STEMI or non-STEMI (< 2 days)
- Severe uncontrolled arrhythmia
- Severe and/or symptomatic obstruction to ventricular outflow
- Decompensated heart failure
- Acute deep vein thrombosis with or without pulmonary embolism
- Acute myocarditis, pericarditis or endocarditis
- Acute aortic dissection
- Intracardiac thrombus with high risk of embolism
- Incapacity to perform physical exercise
- Patient refusal

Relative contraindications^a

- Significant left main coronary artery stenosis
- Ventricular aneurysm
- Supraventricular tachycardia with uncontrolled ventricular rates
- Acquired advanced or complete atrioventricular block
- Recent stroke or TIA
- Hypertrophic cardiomyopathy with severe outflow gradients at rest
- Uncorrected medical conditions, such as marked anemia, significant electrolyte imbalance, hyperthyroidism
- Lack of patient cooperation
- Resting BP > 200/110 mmHg (or lower depending on the patient's age)

BP: blood pressure; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; TIA: transient ischemic attack.

^a At the cardiologist's discretion.

Table 2 Criteria for termination of exercise testing, modified according to [2].**Absolute criteria**

- Severe angina
- Decrease or lack of increase in BP despite workload increase
- ST-segment elevation (not corresponding to a myocardial infarct territory)
- Severe or poorly tolerated arrhythmias: ventricular tachycardia, ventricular fibrillation, second- or third-degree atrioventricular block (complete)
- Signs of low cardiac output: pallor, cold extremities, cyanosis, weakness, dizziness
- Neurological signs: ataxia, confusion, vertigo, etc.
- Technical problems that prevent proper monitoring, electrocardiogram recording and/or BP measuring
- Patient request

Relative criteria^a

- Worsening chest pain
- Marked ST-segment depression ≥ 2 mm or downsloping
- Fatigue or shortness of breath
- Abnormal findings on pulmonary auscultation (crackles, wheezing)
- Leg pain or inability to pursue the exercise
- BP $\geq 250/115$ mmHg
- Less severe and well-tolerated arrhythmias: frequent and/or multifocal PVCs, supraventricular tachycardia, bradycardia
- Bundle branch block

BP: blood pressure; PVC: premature ventricular contraction.

^a At the cardiologist's discretion.

HR response

The HR must increase progressively with exercise intensity. The MHR may be predicted using the Astrand formula: $220 - \text{age} \pm 10$ beats/min established on bicycle [12]. Other

formulae have been proposed with data from treadmill, such as for the general population ($\text{MHR} = 208 - 0.7 \times \text{age}$) [13], for women ($\text{MHR} = 206 - 0.88 \times \text{age}$) [14] and for patients treated with beta-blockers or other bradycardic agents ($164 - 0.7 \times \text{age}$) [15].

Table 3 Assessment of maximal effort, modified according to [9].

Signs of exhaustion and inability to pursue the exercise
Borg scale > 17
Predicted HR reached or exceeded
QR > 1.10 (if CPET)
VO₂ plateau (if CPET)

CPET: cardiopulmonary exercise test; HR: heart rate; QR: VCO₂/VO₂; VCO₂: carbon dioxide output; VO₂: oxygen uptake.

Chronotropic incompetence exists when the actual MHR is ≤ 0 –85% of the predicted MHR – or even 70% – or if $(\text{MHR} - \text{HR at rest}) / (\text{predicted MHR} - \text{HR at rest}) \leq 80\%$ despite a maximal test. Chronotropic incompetence is a marker of poor prognosis and may indicate myocardial ischemia [10,16,17].

During the recovery phase, the HR first decreases rapidly, followed by a slower decline until its return to baseline, which may take several minutes to occur [18]. An HR recovery of ≤ 12 beats/min and ≤ 22 beats/min compared with the MHR, after 1 and 2 minutes, respectively, is considered abnormal, depending on the ergometer used, current treatment and the length and intensity of active recovery [10,19].

BP response

BP must be measured at each step of exercise, despite the challenge in measuring it accurately. For this reason, it should be verified manually. During maximal effort, systolic BP must increase by at least 40 mmHg. During the recovery phase, systolic BP must return to its baseline value or lower, within 6 minutes at most [20–22].

An excessive increase in BP during the first stages may predict an increase in cardiovascular mortality in the long term [23].

A non-increase (< 10 mmHg/MET) or a decrease in systolic BP during exercise constitutes an abnormal finding, often predicting poor prognosis [6,24,25].

Marked hypotension during the immediate recovery may arise, whether symptomatic or asymptomatic; it is usually considered benign [25–27].

Maintaining an elevated BP during the recovery phase seems to indicate altered ventricular function [26,28]. A “systolic BP at 3 minutes of recovery/maximal systolic BP” ratio that is > 0.9 has been suggested as a diagnostic criterion for CAD [26,27].

Exercise electrocardiogram analysis

Repolarization abnormalities

The repolarization abnormalities that most often occur are described in Table 4. The leads involved, the time point at which the abnormality presents and its amplitude and evolution during recovery must all be clearly defined.

Of the repolarization abnormalities, ST-segment depression is by far the most frequent (80–90%); this must be measured 60–80 ms beyond the J point. To be significant, an upsloping ST-segment depression must reach at least 1.5 mm of amplitude at 80 ms. The associated predictive value of a given ST-segment depression is even greater when its amplitude is high, especially with a horizontal or downsloping ST-segment depression [2,29].

Early occurrence of ST-segment depression, the number of leads involved and its persistence during recovery are all in favor of severe coronary lesions [9].

The precordial leads V4, V5 and V6 are affected most frequently by ST-segment depression. However, they do not indicate the precise location of the coronary lesion. Any changes in leads II, III and aVF may be associated with the atrial repolarization wave [9,30].

During the recovery period, exercise-induced ST-segment depression that normalizes early in recovery indicates good prognosis. Inversely, persistence or recurrence of a repolarization abnormality during recovery after its initial disappearance indicates severe CAD [9].

An ST/HR index $> 1.6 \mu\text{V}/\text{beat} \cdot \text{min}^{-1}$ and an ST/HR loop exhibiting a clockwise evolution during the recovery phase indicate the presence of coronary artery lesions with greater accuracy [2,31].

Exercise-induced ST-segment elevation, either isolated or associated with ST-segment depression in a mirror territory, is uncommon. However, it usually indicates the presence of a severe coronary stenosis or a spasm of the corresponding artery, according to the affected territory. Moreover, in postinfarction patients presenting with Q waves, an ST-segment elevation may represent reversible ischemia, dyskinesis or akinetic left ventricular segmental wall motion [9,32,33].

Negative T waves that normalize or occur during exercise, without any ST-segment changes, are of little diagnostic value [9].

Several factors that may affect repolarization must be taken into consideration when interpreting an ET (Table 5) [9].

Table 4 Repolarization changes in favor of myocardial ischemia.

ST-segment depression that is horizontal or downsloping ≥ 1 mm, extending 60–80 ms beyond the J point
Upsloping ST-segment depression ≥ 1.5 mm, extending 80 ms beyond the J point
ST-segment elevation ≥ 1 mm
ST/HR index $\geq 1.6 \mu\text{V}/\text{beat} \cdot \text{min}^{-1}$
ST/HR loop in clockwise fashion

HR: heart rate.

Table 5 Factors modifying the interpretation of repolarization.

Atrial repolarization wave
Repolarization abnormalities on rest electrocardiogram
Arterial hypertension and left ventricular hypertrophy
Wolff-Parkinson-White syndrome
Left bundle branch block
Valvular or congenital heart disease
Mitral prolapse
Cardiomyopathy, pericarditis
Metabolic disorders, hypokalaemia
Digitalis treatment
Treatment with anti-ischemic agents
Other treatments modifying repolarization
Anemia

QRS complex changes

In normal subjects, the QRS duration decreases during exercise, whereas the amplitude of the septal Q wave increases in leads V4, V5 and V6 [2]. An enlargement of the QRS during exercise would be indicative of myocardial ischemia [34–36].

Rhythm abnormalities

An episode of atrial fibrillation during exercise or recovery is predictive of a subsequent sustained arrhythmia—particularly in the elderly [37].

Ventricular arrhythmias depend on the underlying cardiac pathology. The severity of a given ventricular arrhythmia is associated with the QRS complex morphology (polyphasic, polymorphic), its origin, frequency and repetitiveness, as well as with the presence of a short coupling interval (R on T phenomenon) and evolution during exercise. Moreover, worsening of the arrhythmia during an ET, particularly during the recovery period, indicates poor prognosis [38].

Conduction abnormalities

Conduction disorders arising during exercise, such as high-degree atrioventricular blocks, are included in the criteria for ET termination [39].

An underlying cardiac pathology exists in approximately 50% of exercise-induced branch blocks, half of which have an ischemic cause. Left bundle branch blocks arise more often during an ET than right bundle branch blocks [40]. The simultaneous appearance of precordial pain and exercise-induced left bundle branch block may be linked to an asynchronous contraction between the two ventricles [39,41].

Exercise-induced left anterior hemiblock indicates stenosis of either the left main coronary artery or of the proximal interventricular artery, whereas a left posterior hemiblock is a marker for right coronary artery or circumflex artery stenosis, often with extended lesions [35].

Interpretation of the ET in the diagnosis of CAD

For diagnostic purposes, the interpretation of an ET must be multivariable [42,43], and indicate a high, intermedi-

ate or weak probability for myocardial ischemia. Several factors must be taken into account, including disease prevalence, presence of risk factors, symptoms, electrocardiogram changes and possible abnormal changes in HR and BP during exercise and immediate recovery [43,44].

A few scoring systems (Duke Treadmill Score [45], Ashley [46]) aid in the establishment of diagnosis and prognosis of CAD patients, stratifying them into one of the three possible risk groups (Table 6).

CPET data and interpretation

The analysis of a CPET should be based on the pulmonary, cardiovascular and muscular responses to exercise (Table 7). Spirometry before a CPET is mandatory to detect a potential pulmonary limitation. The hemoglobin concentration of the subject must also be taken into account. The CPET interpretation must be structured.

The ET analysis must first be performed as previously described, after which cardiopulmonary data are analyzed with the use of algorithms [7]. All variables are calculated based on three variables: minute ventilation (volume of expired gas [VE], in L/min), and expired oxygen and carbon dioxide fractions (%), measured at each respiratory cycle.

In addition to VO_2 and carbon dioxide output (VCO_2), the main CPET variables used in cardiology include: vital capacity; VE and its components; tidal volume and respiratory rate; breathing reserve; ratio of dead space volume on tidal volume; and partial pressure of end-tidal carbon dioxide (PETCO_2 , in mmHg), reflecting the ventilation-perfusion mismatch.

An abnormal breathing reserve (maximal VE/maximal predicted value of VE) < 30% and a reduction in SpO_2 by > 5% during exercise are useful variables for detecting exercise-induced pulmonary limitation.

In normal subjects, the VO_2 peak value must be $\geq 100\%$ of the predicted value. Interpretation of a reduced VO_2 peak is summarized in Table 7 [47]. The VO_2 peak value is a strong predictor of all-cause mortality and cardiovascular disease, and is therefore one of the most useful prognostic factors in chronic heart failure and many other cardiovascular diseases [11,47].

Beyond the first ventilatory threshold (VT), the VE increases faster than the VO_2 . When comparing the VO_2 value at VT with its value at VO_2 peak (as a %), it is possible to further define the level of physical deconditioning (Table 7). Exercise training increases the VO_2 peak as well as the VO_2 value at VT.

Reduced VO_2 peak and VO_2 at VT (expressed as % of the measured VO_2 peak) favor muscular limitation.

The VE/VCO_2 slope reflects a given patient's respiratory efficiency during exercise. The normal value proposed is a slope < 30, which can increase slightly with age; it is abnormally increased in the context of an inadequate perfusion/pulmonary ventilation balance and has, in addition to VO_2 peak, a strong prognostic value.

The oxygen pulse (VO_2/HR , mL of oxygen/beat), which reflects the left ventricular ejection systolic volume, must increase during the entire exercise duration.

Oscillatory ventilation during exercise represents an abnormal response, mainly observed in patients with chronic heart failure [43].

Table 6 Probability score for coronary artery disease, modified according to [46].

	Men	Women	Score
MHR (beats/min)	≤ 100 = 30 100–129 = 24 130–159 = 18 160–189 = 12 190–220 = 6	≤ 100 = 20 100–129 = 16 130–159 = 12 160–189 = 8 190–220 = 4	
Exercise ST depression (mm)	1–2 = 15 > 2 = 25	1–2 = 6 > 2 = 10	
Age (years)	> 55 = 20 40–55 = 12	> 65 = 25 50–65 = 15	
Angina history	Typical = 5 Atypical = 3 None = 1	Typical = 10 Atypical = 6 None = 2	
Hypercholesterolemia	Yes = 5	NA	
Diabetes mellitus	Yes = 5	Yes = 10	
ET-induced angina	Occurred = 3 Reason for stopping = 5	Occurred = 9 Reason for stopping = 15	
Smoking	NA	Yes = 10	
Estrogen intake status	NA	Positive = –5 Negative = 5	
Total			

ET: exercise test; MHR: maximal heart rate; NA: not applicable. Risk of coronary artery disease for men: Score < 40 = low probability; 40–60 = intermediate probability; > 60 = high probability. Risk of coronary artery disease for women: Score < 37 = low probability; 37–57 = intermediate probability; > 57 = high probability.

Table 7 Interpretation of the main cardiopulmonary exercise test variables, modified according to [7] and [47].

Variables	Normal	Mild impairment	Moderate impairment	Severe impairment
VO ₂ peak / predicted VO ₂ peak (%)	≥ 100	75–99	50–74	< 50
VO ₂ at VT/predicted VO ₂ peak (%)	40–80	< 40		
VE/VCO ₂ slope	< 30	30–35.9	36–45	> 45
Oxygen pulse responses during exercise	Increase	Early plateau or decrease		
Breathing reserve (%)	≥ 30	< 30 ^a		
EOV		Absent	Present	

EOV: exercise oscillatory ventilation; VCO₂: carbon dioxide output; VE: volume of expired gas; VO₂: oxygen uptake; VT: ventilatory threshold.
^a In case of pulmonary disease.

All variables (Table 7) required for the gas exchange analysis must be included in the final report [43].

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Disclosure of interest

The authors declare that they have no competing interest.

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