Cardiopulmonary exercise testing in adult cardiology – expert opinion of the Working Group of Cardiac Rehabilitation and Exercise Physiology of the Polish Cardiac Society

Authors: Krzysztof Smarż, Tomasz Jaxa-Chamiec, Tomasz Chwyczko, Renata Główczyńska, Anna Jegier, Piotr Niedoszytko, Ewa Piotrowicz, Jerzy Rybicki, Ewa Straburzyńska-Migaj, Dominika Szalewska, Sebastian Szmit, Jadwiga Wolszakiewicz

Article type: Expert opinions and position papers

Received: June 25, 2019.

Accepted: June 25, 2019.

Published online: July 4, 2019.

ISSN: 0022-9032

e-ISSN: 1897-4279
EXPERT OPINIONS AND POSITION PAPERS

Cardiopulmonary exercise testing in adult cardiology – expert opinion of the Working Group of Cardiac Rehabilitation and Exercise Physiology of the Polish Cardiac Society

Krzysztof Smarż¹, Tomasz Jaxa-Chamiec¹, Tomasz Chwyczko², Renata Główczyńska³, Anna Jegier⁴, Piotr Niedoszytko⁵, Ewa Piotrowicz⁶, Jerzy Rybicki⁷, Ewa Straburzyńska-Migaj⁸, Dominika Szalewska⁵, Sebastian Szmit⁹, Jadwiga Wolszakiewicz².

¹ Department of Cardiology, Centre of Postgraduate Medical Education, Grochowski Hospital, Warsaw,

² Cardiac Rehabilitation and Non-invasive Electrocardiography Clinic, Institute of Cardiology, Warsaw,

³ Department and Clinic of Cardiology, Medical University of Warsaw, Warsaw,

⁴ Department of Sports Medicine, Medical University of Lodz, Lodz,

⁵ Department and Clinic of Rehabilitation Medicine, Medical University of Gdansk, Gdansk,

⁶ Telecardiology Centre, Institute of Cardiology, Warsaw,

⁷ SPZOZ "REPTY" Upper-Silesian Centre of Rehabilitation, Tarnowskie Gory,

⁸ I Department of Cardiology, University of Medical Sciences, University Hospital of Lord's Transfiguration, Poznan,

⁹ Department of Pulmonary Circulation, Thromboembolic Diseases and Cardiology, Centre of Postgraduate Medical Education, Otwock.
Corresponding author: Krzysztof Smarż, MD, PhD

Centre of Postgraduate Medical Education
Grochowski Hospital, ul. Grenadierów 51/59, 04-073 Warszawa,
e-mail: krzysztofsmarz@hotmail.com, phone/fax: 48-22-810-1738.

<1>Abstract

Cardiopulmonary exercise testing (CPET) is an important diagnostic tool in contemporary clinical practice. This document presents an experts opinion from the Working Group on Cardiac Rehabilitation and Exercise Physiology of the Polish Cardiac Society concerning the indications, performance technique, and interpretation of results for CPET in adult cardiology. CPET is an electrocardiographic exercise test expanded with exercise evaluation of ventilatory and gas exchange parameters. It allows for a global assessment of the exercise performance including the pulmonary, cardiovascular, hematopoietic, neuropsychological, and musculoskeletal systems. It provides a noninvasive dynamic evaluation during exercise and is a reference modality for exercise capacity assessment. This test allows for measuring many prognostic parameters. It is useful in cardiology, pulmonology, oncology, perioperative assessment, rehabilitation as well as in sports medicine and in the evaluation of healthy people. This test not only helps to diagnose the causes of exercise intolerance, but it also supports the evaluation of the treatment. New opportunities are offered by combining CPET with imaging such as exercise stress echocardiography. These tests are complementary and synergistic in their diagnostic and prognostic strength.

Key words: expert opinion; cardiopulmonary exercise testings; exercise testings; diagnostic tests
<2> **Introduction** Cardiopulmonary exercise testing (CPET) is an important diagnostic tool which is increasingly used in cardiology. This test allows to comprehensively evaluate and differentiate the causes of the limited tolerance of exercise. Although this method is becoming increasingly popular, to this date, an unambiguous position of the Polish Cardiac Society was not available. This document presents an opinion of experts from the Working Group on Cardiac Rehabilitation and Exercise Physiology of the Polish Cardiac Society (PCS) concerning the indications, performance technique, and interpretation of results for CPET in adult cardiology.

<3> **Cardiopulmonary exercise testing** CPET is an electrocardiographic exercise test expanded with exercise evaluation of ventilation and gas exchange parameters. The authors of this study proposed a name of cardiopulmonary exercise testing as the most consistent with international nomenclature, although in the literature, there are also other names for this test, i.e. ergospirometry and spiroergometry. In CPET, by measuring direct oxygen uptake, physical capacity can be determined more precisely than during the electrocardiographic exercise test, while all parameters evaluated in the electrocardiographic exercise test can also be measured. [1-4] CPET is increasingly used not only in scientific research but also in daily clinical practice. It is useful in many clinical situations in cardiology, pulmonology and rehabilitation, as well as in sports medicine and in evaluation of healthy people. [5] In CPET, the physical capacity is reflected as maximum oxygen uptake (“maximal aerobic capacity”). It represents the volume of oxygen that a person can uptake from inhaled air within a minute, during physical exercise involving a large part of their muscle mass.

<3> **Historical background** The concept of exercise oxygen uptake goes back to the end of the 18th century. Antoine Lavoisier performed the first measurements of aerobic metabolism during controlled physical exercise in 1790. The first spirometer combined with an ergometer was constructed by H. W. Knipping and L. Brauer in 1929. In 1925, Archibald V. Hill was the
first to describe maximum oxygen uptake (VO\textsubscript{2}max) as the main parameter of cardiopulmonary capacity. CPET was included in the clinical practice in the 1950s.[6] In the 1980s and 1990s, the widespread CPET use in cardiology followed publications of Weber et al. [7] and Mancini et al.[8] which demonstrated a relationship between the disease prognosis and oxygen uptake at peak exercise (VO\textsubscript{2}peak).

**<3>Physiology of exercise**  Physical exercise means any movement of the body effected by skeletal muscles and related to energy expenditure.[9] It requires the coordinated functioning of many systems: cardiovascular, respiratory, musculoskeletal, endocrine, and the nervous system. Based on the nature of muscle contraction, we can distinguish dynamic exercise in which the length of muscles changes during the contraction and work is performed, and static exercise, in which the muscle tension increases, but the length remains unchanged.[10] In natural conditions, the exercise is usually of a mixed character.

A direct measure of exercise intensity is the amount of oxygen consumed by working muscles. Based on volumes of oxygen uptake (VO\textsubscript{2}) and carbon dioxide output (VCO\textsubscript{2}) per time unit, biochemical processes occurring at the tissue level can be evaluated. Oxidation of organic substances in the body provides roughly the same amount of energy as their combustion outside the body; it also requires the same amount of oxygen. Consumption of 1 L of oxygen provides 19.6 kJ when fats are burned, and 21.1 kJ when carbohydrates are processed (a difference of 10%)[10]. Below the anaerobic threshold (AT), oxygen and carbon dioxide volumes measured at the mouth level correspond to volumes of these gases at the tissue level. The respiratory exchange ratio (RER) is measured by VCO\textsubscript{2}/VO\textsubscript{2} at the mouth level and reflect a carbon dioxide production and oxygen consumption quotient at the tissue level - metabolic respiratory quotient (QCO\textsubscript{2}/QO\textsubscript{2}, RQ). In the steady state, when there is no hyperventilation or uncompensated metabolic acidosis, RER = RQ. Glucose is oxidised at RQ = 1.0 (e.g. 6 molecules of CO\textsubscript{2} are produced, and 6 molecules of O\textsubscript{2} are consumed). When 1
glucose molecule is oxidised in the oxidative phosphorylation process, 36 molecules of adenosine triphosphate (ATP) are regenerated from adenosine diphosphate (ADP) in the presence of phosphocreatine (PCr), and the ratio of ATP molecules to oxygen molecules is 6.0 (36 ATP/6 O\textsubscript{2}). Fats (e.g. palmitate) are oxidised at RQ = 0.71 (e.g. 16 molecules of CO\textsubscript{2} are produced, and 6 molecules of O\textsubscript{2} are consumed). When 1 molecule of palmitic acid is oxidised, 130 molecules of ADP are rephosphorylated to ATP, and the ratio of ATP molecules to oxygen molecules is 5.65 (130 ATP/23 O\textsubscript{2}).[11] RQ values are in a steady state, reflecting the corresponding rates of carbohydrates and fats used in metabolic processes. The use of individual substrates during physical exercise depends on its intensity and duration.

During light exercise (30-40% VO\textsubscript{2} max), the primary source of energy is glucose from hepatic glycogen and free fatty acids. During moderate exercise (50-70% VO\textsubscript{2} max), muscle glycogen and free fatty acids are consumed. During highly intense exercise (>70% VO\textsubscript{2} max), muscle glycogen resources are used mainly in the mechanism of anaerobic glycolysis, and this leads to an increased level of lactates. RQ at rest is ca. 0.8, and during moderate exercise, it increases up to 0.95 (at this RQ value, ca. 84% of energy comes from carbohydrates).[11] Bergstrom et al. demonstrated a positive relationship between intense exercise duration and the glycogen content in muscles before the exercise.[12] More physically fit people use fats at a higher rate during exercise, thus delaying depletion of glycogen resources and fatigue. Because stores of fat are larger, they are a better energy substrate, while carbohydrates are more efficient. Sources of glucose include glycogen stored in muscles and plasma glucose from glycogen degradation in the liver, while source of free fatty acids are triglycerides stored in muscles and fatty tissue. Proteins are used solely during starvation and prolonged physical exercises when glycogen is exhausted.

In humans, the skeletal mass represents ca. 38% of total body weight, so for the body weight of 70 kg this corresponds to ca. 27 kg.[13] Skeletal muscles contain three types of muscle
fibres: I, IIa and IIx. This classification is based on their biochemical properties and contractility. Type I is called slow oxidative (SO) fibres, and are characterised by the red colour of fibres and slowly increasing tone (ca. 80 ms). Type IIa fibres are fast oxidative-glycolytic (FOG) fibres, and type IIx are fast glycolytic fibres. Type IIa and IIx fibres are called fast twitch fibres, with their tone increasing very fast (about 30 ms). Type I fibres are characterised by a higher content of mitochondria and a higher level of myoglobin containing iron (hence their red colour), they also contain more oxygen-processing enzymes, and enzymes associated with the oxidation of fatty acids. Type II fibres, on the other hand, are white due to their lower content of haemoglobin, contain fewer mitochondria and higher levels of anaerobic-processing enzymes. Type I fibres contract slower but are more resistant to fatigue, while type II fibres contract fast but their resistance to fatigue is lower. The distribution of different types of fibres in human skeletal muscles is different in different muscle groups. Proportions of fibre types in muscles vary, depending on physical activity. In long-term immobilisation or reduction in physical activity due to chronic disease, a shift towards type II fibres occurs. Exercise of low intensity involves recruitment of mainly type I fibres, while type II fibres are recruited during heavy loads, especially those exceeding 70–80% of oxygen capacity.[11]

ATP generated during the oxidation of energy compounds is used for changes in the internal configuration of actin and myosin, reflected as muscle shortening or increased tension. The effectiveness of muscle cells depends on ATP supply and possibilities for its regeneration. The amount of ATP stored in the rested muscle is sufficient for only 1–2 seconds, so it has to be constantly renewed during exercise. Biochemical processes used to replenish stores of cellular ATP include glycolysis with generation of pyruvate or (in anaerobic conditions) lactate, oxidative phosphorylation in the respiratory chain, in which pyruvate, free fatty acids,
and ketone bodies are used as substrates, phosphocreatine transformation into creatinine, and ATP synthesis from two ADP molecules.[14]

Even before the dynamic exercise begins, the cardiac output is increased due to a reduction of the vagal tone. This way, the body is prepared for physical activity. Oxygen uptake by the cardiac muscle depends on the wall tension, contractility, heart rate (HR), and, to a lesser extent, on external work, energy required for activation, and basic cardiac metabolism. In physiological conditions, cardiac metabolism is solely aerobic. Energy substrates for the cardiac muscle include glucose, free fatty acids, lactic acid and ketone bodies. An increase in the venous blood flow to the heart causes the following changes in haemodynamic parameters: an increase in the end-diastolic volume of atria and ventricles, an increase in ventricular diastolic pressure due to greater filling of the ventricles, an increase in atrial diastolic pressure due to the increased inflow and higher ventricular diastolic pressure; an increase in atrial and ventricular contractile strength leading to an increase in the stroke volume (SV), and thus, in the cardiac output.

The greatest (80%) oxygen consumption by the cardiac muscle occurs during an isovolumetric contraction. In that period, the cardiac energy expenditure depends on the afterload, end-diastolic pressure, and the rate of the wall tension increase. The oxygen uptake by the cardiac muscle is increased by the stimulation of the sympathetic system, and reduced by the activity of the parasympathetic system. During exercise, HR accelerates first due to the inhibition of the parasympathetic system, and then by the stimulation of the sympathetic system. Additionally, the increase of the sympathetic tone causes contraction of veins and arteries in most organs, excluding working muscles, the central nervous system, and the coronary circulation. The above reactions increase ventricular filling volume and accelerate HR. During exercise, the systolic blood pressure (SBP) increases, while the diastolic blood pressure (DBP) remains the same or is slightly reduced. The cardiac index changes within a
range from 3.5 L/m²/min at rest to 22 L/m²/min during exercise. Its increase is caused by a mechanism dependent on cardiac stretch (according to the Frank-Starling law) and a mechanism dependent on the nervous regulation of its rate and contractility.[15]

During exercise, the respiratory system is to supply the sufficient amount of oxygen to cover the increased metabolic demand, and to remove the generated carbon dioxide on a regular basis. Through the elimination of carbon dioxide, it also affects acid–base homoeostasis.

During exercise, the minute ventilation of the lungs increases; initially, due to the increased tidal volume (VT), and then (>60–70% of the maximum load) due to increased breathing frequency (BF). In physiological conditions, minute ventilation does not reach the maximum voluntary ventilation (MVV), and if there is no respiratory disease, its function does not limit the exercise capacity.

Fatigue during exercise, apart from a subjective perception, is reflected in a reduced rate and strength of muscle contractions. It can be caused by myocyte acidity (accumulation of hydrogen ions) leading to reduced calcium release and binding to myocyte contractile components or by a drop in ATP levels caused by dominance of its consumption over production.[16]

**Physical capacity** Physical capacity (exercise capacity, exercise tolerance) is understood as maximum fatigue caused by physical exercise that is tolerated by the patient.[17] It is the capability to perform aerobic exercise determined by maximum oxygen uptake. In practice, it means the ability to conduct daily activities based on aerobic metabolism.[18] This term also covers tolerance of fatigue-related metabolic changes and the ability to quickly eliminate them when the work is completed.[19]

Physical capacity evaluated in CPET means the cardiopulmonary (aerobic) capacity, being a component of a widely understood physical fitness. Physical fitness comprises of capacity dependent on the health status (cardiopulmonary capacity, muscular endurance, muscular
strength, body composition, and flexibility) and capacity dependent on skills (agility, balance, motor coordination, speed, power, reaction time).[9] The maximum exercise is evaluated in relation to its intensity and duration. The exercise intensity can be measured in units of power (watt) or as energy expenditure, measured as oxygen uptake during exercise [L/min]. In case of electrocardiographic exercise tests conducted on a treadmill, metabolic equivalents of task (MET) are used to evaluate exercise intensity, calculated using the equations proposed by the American College of Sports Medicine (ACSM), taking into account the treadmill speed and incline.[20] One MET corresponds to the consumption of 3.5 millilitres of oxygen per kilogram of body weight per minute. That value was established based on oxygen uptake at rest by a 40-year-old man of body weight of 70 kilograms. An estimated capacity evaluation with MET, based on the treadmill speed and incline, can lead to an overestimated capacity rate. Ades et al. demonstrated that capacity values were overestimated by 30% in men and 23% in women when oxygen uptake was calculated from MET, when compared to a direct measurement of VO$_2$peak.[21]

Physical capacity depends on age, sex, as well as body weight and body composition. It is assumed that human aerobic physical capacity increases up to 20 years of age, then it is stabilised between 20 and 25 years of age, and after 25 years of age it regularly declines on average by 10% per each decade of life. Fleg et al. demonstrated that physical capacity decreases by 3–6% per every 10 years in young (20–30 years) and by up to > 20% in older (>70 years) healthy people.[22] At every age, physical capacity of women is 10–20% lower than that of men. This is related to their lower muscle mass, lower haemoglobin concentration, and smaller SV.[18] The age-dependent decrease in physical capacity is associated with a progressive reduction in muscle mass, SV and maximum achievable HR. Reduction in SV results from the decreasing contractility of muscle fibres and their defective relaxation. Regular physical activity may slow this process down.[23]
Factors underlying capability for aerobic physical exercise:

1. Effectiveness of functions jointly facilitating oxygen transport to the tissues (maximum cardiac output, arterial-mixed venous oxygen content difference, haemoglobin level, diffusing capacity of the lung, maximum lung ventilation),
2. Age, sex, genetic factors,
3. Physical training, daily physical activity,
4. Thermoregulatory effectiveness,
5. The efficiency of systemic mechanisms controlling metabolism, including the capacity of buffer systems reducing acidosis and processing lactate,
6. Tolerance of fatigue changes: mental factors, tolerance of hypoglycaemia,
7. Musculoskeletal system characteristics.

Direct measurement of oxygen uptake with its value referred to the norms for a population (relative capacity) taking into account race, sex, age, and body composition, is considered as a reference parameter for evaluation of physical capacity.

<2>Indications and contraindications Indications for CPET in cardiology [1,2,5,11,24-27]:

1. Establishing causes of exercise intolerance and dyspnea;
2. Diagnostics, evaluation of the disease progression, exercise capacity and prognosis in:
   - Heart failure, hypertrophic cardiomyopathy, pulmonary hypertension, suspected ischaemic heart disease, suspected mitochondrial myopathy, unexplained exertional dyspnoea,
   - Chronic obstructive lung disease or interstitial lung disease, pre- and post-operative evaluation and evaluation of long-term prognosis, valvular diseases,
3. Evaluation of physical capacity in apparently healthy people,
4. Choice of training, monitoring, and evaluation of results in cardiac rehabilitation
5. Evaluation of treatment effectiveness.
Contraindications to CPET, direct and conditional indications to stop the testing are the same as for electrocardiographic exercise testing, and are described in a separate document.[28]

<2>Technical conditions and preparing equipment for tests

Technical conditions, equipment, and safety requirements to be met by the room, where CPET is performed do not differ significantly from those specified for electrocardiographic exercise testing and are described in a separate document.[28]. Additionally, the room should be equipped with a hygrometer and an indoor thermometer. For cardiopulmonary exercise evaluation, the system for exercise testing should be additionally equipped with a gas analyser and a set of face masks (of various sizes to match the patient’s face ensuring its tightness). Optionally, appropriate mouthpieces and a nose clip can be used instead of a mask.

Before the testing, the apparatus must be calibrated, taking into account current environmental conditions, as specified in instructions provided by a manufacturer. Volumetric calibration with a standard 2–3 litre syringe (depending on the recommendations of a manufacturer) need to be adjusted to BTPS conditions (body temperature, pressure, saturated with water vapour - temperature of 36.8°C, atmospheric pressure, 100% humidity). Gaseous calibration should be performed using a standard gas mixture containing 15% of oxygen, 6% of carbon dioxide and 79% of nitrogen. Gaseous parameters should be adjusted to STPD conditions (standard temperature, pressure, dry - temperature of 0°C, pressure of 1013 hPa, 0% humidity).

<2>Supervising personnel  CPET should be supervised and interpreted by a doctor with experience in exercise testing specified in a separate document [28], additionally, with knowledge and experience in performance and interpretation of cardio-pulmonary results.[1]

<2> Conducting the test <3> Indications for the test
Before the CPET, the indication for the test should be established based on a referral and medical history.

**Patient medical history**
A pertinent review of systems in the week preceding the test including basic problems, their intensity (e.g. increasing coronary pain, significant abrupt drop in the exercise capacity, syncope at rest and on exertion), as well as relevant past medical history (e.g. recent or existing infections, orthopaedic and neurological disorders, or mental diseases, such as depression or anxiety) should be elicited. Patient’s exercise capacity based on the daily activity and ability to perform physical exercise (for instance according to NYHA class) should be assessed before the test. Names and doses of cardiac medications, as well as the time of the last dose taken on the day of the test should also be noted.

**Patient data and protocol selection**
In accordance to the rules described for electrocardiographic exercise testing.[28]

**Information about the test and a written consent**
Before the test, the patient should be informed about the aim and the procedure of the test, and about possible inconveniences and complications related to the test. Written consent must be obtained.

**Patient preparation**
A patient should come for the test about 3 hours after a light meal in comfortable, loose clothing and sports footwear enabling walking on a treadmill or riding an exercise bike. For up to 6 hours before the test, the patient should avoid intense physical exercise, should not drink strong tea or coffee, or any other energy drinks, or smoke cigarettes. On the day of the test, the patient should take their standard medications. Before the test, communications techniques about fatigue, any undesirable symptoms, and the need to stop exercise, should be established.

**Skin preparation and placement of leads**
Skin preparation and leads placement was described previously in separate document.[28]

**Conducting the test**
**Test stages, loading protocols**
Before the exercise is started, the performance of spirometry at rest is recommended, and in the majority of devices is necessary.

The CPET stage should include: warming up (2–3 minutes), exercise (about 8 to 12 minutes), recovery phase (5 minutes or to resolution of electrocardiographic changes and/or clinical symptoms).

For CPET ramp and customised protocols are recommended. A detailed description of available protocols and methods for customised protocols were described in recommendations for electrocardiographic exercise testing.[28]

**Variables measured during cardiopulmonary exercise testing** During CPET and immediately after its completion, all parameters evaluated during electrocardiographic exercise testing (clinical, haemodynamic and electrocardiographic), as well as ventilatory and gas exchange variables should be assessed. Parameters evaluated in electrocardiographic exercise testing are described in a separate document.[28]

**Ventilatory parameters:**
1. minute ventilation (VE) [L/min],
2. tidal volume (VT) [L],
3. breathing frequency (BF) [L/min],
4. breath reserve (BR) [%],
5. dead space volume to tidal volume ratio (VD/VT),
6. ventilatory efficiency - ventilation versus carbon dioxide slope (VE vs VCO₂ slope).

**Gas exchange parameters:**
1. oxygen uptake at peak exercise (VO₂ peak) [ml/kg/min, L/min], percent of predicted oxygen uptake at peak exercise, (% VO₂ pred) [%],
2. oxygen uptake at anaerobic threshold (VO₂-AT) [ml/kg/min, L/min],
3. oxygen pulse (O₂ pulse) [ml/beat], percent of predicted oxygen pulse O₂ pulse [%],
4 oxygen uptake plotted against work rate (WR) increase,
5 $O_2$ pulse plotted against WR increase,
6 carbon dioxide output ($VCO_2$) at peak exercise [L/min],
7 respiratory exchange ratio (RER),
8 ventilatory equivalent for oxygen (EQO$_2$),
9 ventilatory equivalent for carbon dioxide (EQCO$_2$),
10 end-tidal oxygen partial pressure (PETO$_2$) [mm Hg],
11 end-tidal carbon dioxide partial pressure (PETCO$_2$) [mm Hg],
12 oxygen uptake efficiency slope (OUES).

<2>Parameters of cardiopulmonary exercise testings and their interpretation<3>

**Oxygen uptake**  Oxygen uptake ($VO_2$) during physical exercise is a measure of aerobic capacity. $VO_2$ depends on the cellular oxygen demand and the ability to transport oxygen to tissues. Oxygen availability for tissues is influenced by: gas exchange at the alveolar level (structure and function of the respiratory system), blood ability to transport oxygen (haemoglobin concentration, arterial blood saturation, haemoglobin dissociation curve, carbon dioxide content, pH of blood), heart function (HR, SV), peripheral blood redistribution, oxygen extraction by tissues (capillary thickness, mitochondrial density and function, perfusion, tissue function).

$VO_2$ is defined as the product of the stroke volume and the arterial-mixed venous oxygen content difference: $VO_2 = HR \times SV \times [C(a - v)O_2]$, HR – heart rate, SV – stroke volume, $C(a - v)O_2$ – arterial-mixed venous oxygen content difference [mL O$_2$/dL of blood].

During exercise, $C(a - v)O_2$ is linearly correlated with $VO_2$ and achieves a physiological limit of 12 - 16 mL O$_2$/dL of blood depending on the haemoglobin concentration (12 - 16 g/dL) therefore, $VO_2$ at peak exercise depends mainly on the stroke volume. [29-31]
Oxygen consumption during exercise with an increased load rises slowly until it reaches a plateau. VO2 may increase fifteen times from rest values of 3.5 ml/kg/min, to 30-50 ml/kg/min. In well-trained people VO2 may be even twenty times higher and reach 94 ml/kg/min.[1,2]

VO2 at peak exercise may be expressed as maximum oxygen uptake (VO2max) or peak oxygen uptake (VO2peak). VO2max represents the amount of oxygen uptake during maximum physical exercise and is defined as the lack of increase in VO2 (plateau), despite the increasing load at maximum fatigue. VO2max is achieved in healthy people that can perform maximum exercise. The time to achieving VO2 max depends on the dynamics of the load increase (protocol). The greater the load increase in time, the sooner is VO2 max achieved. However, in each case, the VO2 max value is the same. In healthy people, VO2 increase versus load increase (VO2/WR) is 10 ml/min/watt, on average.[31] Obesity shifts the VO2-WR relationship to a higher level, without changing the VO2 increase rate. VO2 course versus WR is steeper in well-trained individuals, and flatter in those with cardiovascular diseases.[32]

In patients with cardiovascular or respiratory diseases, reaching VO2max is impossible (and may be dangerous); therefore, in this group, VO2peak evaluation is used instead. It represents oxygen uptake at the peak of the exercise, usually at fatigue of 15–16 points on the 20-point (or 5–6 points on the 10-point) Borg scale. VO2 max or VO2 peak should be presented as absolute [ml/min, L/min] and relative, calculated per kilogram of the patient’s body weight [ml/kg/min] values. Lower VO2peak may reflect problems with oxygen transport (stroke volume, blood ability to bind and transport oxygen), lung function (obturation, restriction, gas exchange), oxygen extraction at the tissue level (tissue perfusion and diffusion), neuromuscular and skeletal muscle disorders, and insufficient physical exercise.

<4> Maximum test criteria.
There is no “gold standard” for the evaluation of maximum physical exercise. During CPET, presence of one or more of the following criteria is considered as features of maximum exercise [2,33,34]:

1. achieved plateau of VO\(_2\) and/or HR despite continued load increase,
2. peak respiratory exchange ratio, RER ≥ 1.10,
3. post-exercise lactate concentration ≥ 8 mmol/L,
4. perceived exertion ≥ 18 (Borg 6-20) or ≥ 8 (Borg 0-10),
5. exhaustion.

**Predicted oxygen uptake** To reduce interindividual variations, VO\(_2\) peak should be expressed as a percent of predicted oxygen uptake at peak exercise (%VO\(_2\)pred). VO\(_2\) depends on the studied population, age, sex, body size, fat free body mass, level of daily physical activity, and the loading conditions. For the above reasons, the physical capacity of an examined person may differ from the calculated predicted value. To calculate the predicted oxygen uptake value (VO\(_2\)pred), the following is recommended according to the opinion of the American Thoracic Society/American College of Chest Physicians (ATS/ACCP) and the European Association for Cardiovascular Prevention & Rehabilitation/American Heart Association (EACPR/AHA) equations according to Wasserman/Hansen [1,5,35].

Method for VO\(_2\)pred calculation in men and women are presented in Table 1 and 2.

[27,35,36]

**Carbon dioxide output** Carbon dioxide output (VCO\(_2\)) during exercise depends on stroke volume, blood ability to transport carbon dioxide, and tissue exchange. As carbon dioxide is 20 times more soluble in blood than oxygen, VCO\(_2\) measured at the mouth level depends to a greater extent on ventilation than it is the case for VO\(_2\). Additionally, the body uses carbon dioxide production to compensate for metabolic acidosis. Therefore, VCO\(_2\) increases significantly when the anaerobic threshold is exceeded.
Respiratory exchange ratio  The relationship between VCO₂ and VO₂ is called the respiratory exchange ratio (RER). It is calculated as a ratio between VCO₂ and VO₂ (VCO₂/VO₂). Carbon dioxide output and oxygen uptake increase at the same rate to RER = 1.00. Above that value, VCO₂ is additionally caused by an increased carbon dioxide production due to lactate compensation and hyperventilation. RER of ≥ 1.10 at peak exercise is a generally accepted indicator of sufficiently great fatigue during the test; however, exceeding this value is not an indication for discontinuing the exercise. Reaching of RER < 1.00 at the peak of the exercise reflects submaximal exercise, and can also be observed in some pulmonary restrictions of exercise tolerance.[25]

Anaerobic threshold  Anaerobic threshold (AT) represents such level of exercise above which aerobic production of energy is supported by anaerobic processes and is reflected in an increase in lactate levels in tissues and in peripheral blood. AT can be defined physiologically as VO₂, above which aerobic ATP production in muscles is supplemented by anaerobic processes. Oxygen uptake at AT (VO₂-AT) is expressed as a percentage of VO₂pred and as a percentage of VO₂peak.[5,35] The mean value of VO₂-AT in people that do not train and lead a sedentary lifestyle, is within the range of 50–60% VO₂pred. In the general population of healthy people, VO₂-AT is within an extensive range of 35–85% and depends on age, exercise type, and load protocol. VO₂-AT is independent of the patient’s motivation to exercise. The time of AT development depends on the metabolism of working muscles. VO₂-AT can be reduced by the same disorders as VO₂peak.

Determination of the anaerobic threshold  Both invasive and non-invasive methods are used to determine AT. In the invasive method, lactate levels in the peripheral blood are determined. This way, the lactate thresholds are established – first at the lactic acid level > 2 mmol/L, and second at the lactic acid level > 4 mmol/L.
In CPET, AT is usually determined by a non-invasive method, by determining the ventilatory thresholds VT1 (first ventilatory threshold) and VT2 (second ventilatory threshold), also called the respiratory compensation point (RCP). VT1 is usually determined by the V-slope method or by the ventilatory equivalents method, while the ventilatory equivalents method is used for VT2.

The V-slope method uses a curve of VCO₂ in relation to VO₂. An increase in the VCO₂ rise rate versus VO₂ results in a steeper curve. AT is found at the curve bending point.

The ventilatory equivalents method uses the time course of respiratory equivalents for oxygen (VE/VO₂) and carbon dioxide (VE/VCO₂) and end-tidal partial pressure for oxygen (PETO₂) and carbon dioxide (PETCO₂). AT is determined at the point, at which VE/VO₂ and PETO₂ reach their minimum, and their steady increase begins, while VE/VCO₂ and PETCO₂ remain unchanged.

It is recommended to determine AT with the above methods, optimally applying both methods simultaneously (dual methods approach), with concurrent RER evaluation, which should be close to 1.0.

**Oxygen pulse** Oxygen pulse (O₂pulse) is a product of VO₂ and HR presenting the amount of oxygen inhaled per one heartbeat (VO₂/HR) [ml/beat].

According to the Fick equation, VO₂ depends on stroke volume and the arterial-mixed venous oxygen content difference. Therefore, changes in O₂pulse during exercise reflect changes in SV. O₂pulse = SV x [C(a – v)O₂], were SV indicates stroke volume, C(a – v)O₂ indicates arterial-mixed venous oxygen content difference [mL O₂/dL of blood].

In normal conditions, O₂pulse increases during incremental load exercise, assuming the shape of hyperbola, with a fast increase at low exercise intensity and gradual flattening at peak exercise.
Low O$_2$ pulse, unchanging despite the increase in the load, may result from a reduced SV and/or tissue inability for further extraction of oxygen. Low O$_2$ pulse may reflect poor physical fitness, cardiovascular diseases or reduced capacity caused by lung diseases.

**Maximal voluntary ventilation** Before the exercise testing, spirometry at rest should be performed, to evaluate vital capacity (VC) and forced expiratory volume in one second (FEV1). Spirometry at rest allows excluding significant restriction or obturation which can result in exercise limitation. The spirometry result is used to calculate the maximum voluntary ventilation (MVV) from the equation:

\[
\text{MVV} = \text{FEV1} \times 40.
\]

Detailed description of spirometry exceeds the scope of this publication.

**Breathing reserve** Exercise breathing reserve (BR) shows the extent to which the minute ventilation (VE) approaches MVV at peak exercise, and can be expressed as litres per minute (BR [L/min] = MVV [L/min] – VE peak [L/min]) or as a percentage (BR [%] = \{ (MVV [L/min] – VE peak [L/min]) / MVV [L/min] \} x 100%).

BR value of 15% represents the lower limit of a normal range in an average population of healthy people. Athletes (due to their high exercise capacity) and elderly people (due to low MVV) can have lower BR values even when no disease is present.

Exercise breath reserve can also be expressed as the product of peak ventilation multiplied by maximum voluntary ventilation at rest (VE peak/MVV) or its percentage ratio (100 x VE/MVV). Predicted values of these parameters are 0.8 and below, and 80% and below, respectively.[1,5] In healthy people, VE at peak exercise is within the range of 50–80% MVV.
**Breathing frequency**  Breathing frequency (BF) represents the number of breaths per minute. In the majority of people, BF increases 2 to 3 times, and in healthy people it does not exceed 50 to 60 breaths per minute.

**Tidal volume**  Tidal volume (VT) represents the volume of one breath. During exercise, VT increases 3–4 times in younger and 2–4 times in older people.

**Minute ventilation**  Minute ventilation (VE) is the product of VT and BF: $VE = VT \times BF$. VE rises progressively during exercise, initially due to VT increase to 60–70% of the maximum load, and then mainly due to an increase in BF. In heart failure patients, the VE versus load curve may oscillate.

**Exercise oscillatory ventilation**  Exercise oscillatory ventilation (EOV) means alternate hyper- and hypoventilation. The diagnosis is based on determining parameters of oscillatory ventilation for at least 60% of the exercise duration, of amplitude of $\geq 15\%$ of the average VE value at rest.[26]

**Ventilatory equivalent for oxygen**  Ventilatory equivalent for oxygen (VE/VO$_2$) is the VE to VO$_2$ ratio. It represents the volume of minute ventilation required to uptake 1 litre of oxygen. This parameter is non-linear. Its value is influenced by intensified ventilation, increased dead space volume, and oscillatory breathing.

**Ventilatory equivalent for carbon dioxide**  Ventilatory equivalent for carbon dioxide (VE/VCO$_2$) is the VE to VCO$_2$ ratio. It represents the volume of minute ventilation required to output 1 litre of carbon dioxide. This parameter rises during hyperventilation and when the dead space volume increases. In physiological conditions, 23 to 25 litres of VE is required to output 1 litre of CO$_2$. The mutual relation of courses of VE/VO$_2$ and VE/VCO$_2$ curves allows to differentiate the cause of intensified ventilation (metabolic acidosis, psychiatric disorders, anxiety).
**Oxygen and carbon dioxide end-tidal partial pressure**
Oxygen (PETO$_2$) and carbon dioxide (PETCO$_2$) partial pressure are measured at the end of spontaneous exhalation. These parameters depend on hyperventilation and dead space volume. During exercise, initially, PETO$_2$ decreases and PETCO$_2$ increases, with further load, PETO$_2$ decreases, reaching the lower turning point (nadir), and PETCO$_2$ remains unchanged (AT, simultaneous increase in VE/VO$_2$). During further loading, PETO$_2$ continues to rise, while PETCO$_2$ starts to go down (with a simultaneous increase in VE/VCO$_2$) – indicating that the respiratory compensation point has been reached.

**Physiological dead space volume to tidal volume ratio**
The physiological dead space volume to tidal volume ratio (VD/VT) indicates a fraction of each breath corresponding to dead space volume – anatomical (oral cavity, larynx, bronchi) and functional (poorly perfused alveoli). VD/VT reflects a disrupted balance between ventilation and perfusion. In healthy people, VD/VT is about 0.34 and decreases by 0.1 during exercise. In patients with lung diseases or pulmonary hypertension caused by diseases of the left heart, this parameter is higher and does not decrease during exercise. Calculation of this parameter requires an invasive measurement of CO$_2$ partial pressure in the arterial blood, PaCO$_2$, and calculation of the mixed CO$_2$ partial pressure in the expiratory air, PETCO$_2$, as well as taking into account the dead space volume of the apparatus. The use of “non-invasive” method for VD/VT calculation, using PaCO$_2$ estimation based on normal ratios of expiratory gases during exercise in healthy people [37], may be a source of error in the diagnostics of the significantly disrupted ventilation to perfusion rate in patients with such diseases.[1]

**Ventilatory efficiency**
Ventilatory efficiency is measured as ventilation versus carbon dioxide slope (VE vs VCO$_2$ slope). It represents a relationship between VE and VCO$_2$ expressed as the slope of the straight line calculated using a simple linear regression.
equation.[38] With the increased ventilation, as in the case of heart failure patients, VE vs VCO$_2$ slope is steeper than in healthy people. Normal values are within the range of 20–30.

**Oxygen uptake efficiency slope** The oxygen uptake efficiency slope (OUES) characterises the respiratory response to physical exercise. It represents an absolute increase in VO$_2$ related to the tenfold increase in ventilation. It is presented as a linear relationship between VO$_2$ and VE decimal logarithm.

**Results interpretation, final report and conclusions** The approach to the interpretation of the results of the test should be comprehensive and integrated.

In the test evaluation, the following should be considered:

1 indication for the examination,
2 clinical details, results of additional tests, medications taken, level of physical activity,
3 comparison of numerical test results to reference values,
4 graphic charts (e.g. a panel of 9 charts according to Wasserman),
5 clinical presentation (chest pain, dyspnoea, general fatigue, lower extremity muscle fatigue),
6 HR, blood pressure and electrocardiographic changes,
7 perceived exertion,
8 reason for test termination.

The main parameters measured during CPET and criteria of a normal response to exercise are shown in Table 3.[5]

The charts proposed by Wasserman - the 9 panels plot, presenting relationships between parameters evaluated during CPET, are most commonly used.

In the fifth edition of the textbook *Principles of Exercise Testing and Interpretation* published in 2012, the order of the panels and some parameters were changed. Graphic presentation of parameters aims at facilitating the interpretation of the study result.[35,39]
A 9 panels plot according to Wasserman (of 2012):

1. panel 1: VO$_2$, VCO$_2$, WR (y-axis) versus time (x-axis) and a line presenting VO$_2$pred and the predicted VO$_2$ increase versus the WR increase,
2. panel 2: HR and O$_2$ pulse (y-axis) versus time (x-axis),
3. panel 3: HR (y-axis) versus VO$_2$ (x-axis) and VCO$_2$ (y-axis) versus VO$_2$ (x-axis),
4. panel 4: EQO$_2$ (VE/VO$_2$) and EQCO$_2$ (VE/VCO$_2$) (y-axis) versus time (x-axis),
5. panel 5: VE (y-axis) versus time (x-axis),
6. panel 6: VE (y-axis) versus time VCO$_2$ (x-axis), scale 30:1,
7. panel 7: PETCO$_2$, PETO$_2$, SpO$_2$ (y-axis) versus time (x-axis),
8. panel 8: RER (VCO$_2$/VO$_2$) (y-axis) versus time (x-axis),
9. panel 9: VT (y-axis) versus VE (x-axis); The vital capacity (VC) and the inspiratory capacity (IC) are shown as horizontal lines. MVV is shown as a vertical line.

First, on the basis of VO$_2$ peak, the patient is evaluated for limitations in physical capacity (panel 1). When VO$_2$ peak is lower, the cause is determined – whether it is cardiac (panels 1, 2 and 3), or respiratory (panels 1, 5, 7 and 9), or related to disrupted ventilation to perfusion rate (panels 1, 4, 6 and 7), or to metabolic disorders (panels 1 and 8).

The evaluation of results should help in answering a number of questions presented in Table 4.[31]

Methods used to diagnose the causes of limited exercise tolerance caused by cardiovascular or respiratory diseases are based on algorithms. Algorithms proposed by Wasserman are most commonly used.[40] A simplified diagnostic algorithm is shown in Figure 1.[27,40] Coloured algorithms proposed by Guazzi M. and Arena R. et al., separate for individual diseases or syndromes, are useful in practice when the disease stage and prognosis are evaluated.[5,26]

A final report should include:
patient details, age, body weight, height,

test date,

indications for the test,

initial diagnosis and treatment,

type of equipment/apparatus used in the test (treadmill, bicycle ergometer), loading protocol,

perceived exertion (Borg scale),

reason for test termination,

HR and blood pressure responses to the load, and electrocardiographic changes,

main parameters of spirometry at rest,

graphical data display,

numerical data (initial, at peak exercise, at AT and at RCP (when determined), and % of predicted values);

descriptive results interpretation: presence, degree and possible cause of the capacity limitation;

comparison to previous results (when available).

Clinical applications and interpretation of cardiopulmonary exercise testing

Exertional dyspnoea - distinguishing between cardiac and pulmonary causes

Cardiovascular and respiratory diseases are the most common causes of exertional dyspnoea and limited exercise tolerance. CPET allows an integrated evaluation of the response of the respiratory and circulatory system to exercise. Evaluation of exertional dyspnoea of unspecified origin is a fundamental indications for CPET. Differentiation is challenging, especially when these disorders are not advanced, and they are caused by heart failure with preserved ejection fraction (HFpEF), or even a more difficult case when heart failure is accompanied by chronic obstructive pulmonary disease (COPD). It is estimated that
up to 40% of heart failure patients have COPD and ca. 30% of COPD patients have heart failure.[5,25,27]

The main parameters evaluated in differential diagnosis of dyspnoea are: VE vs VCO₂ slope, % VO₂pred, PETCO₂ and BR. Spirometry should be performed both before and after CPET (particularly, in evaluation of exercise-induced asthma), with an evaluation of FEV1 and the peak expiratory flow (PEF). Pulse oximetry (SpO₂) should also be monitored.

To detect exercise induced bronchospasm (EIB), usually intensified during the first several minutes after exercise, FEV1 and PEF measurements should be performed 1, 3, 5, 7, 10, 15 and 20 minutes after CPET completion. Reduction in FEV1 > 15% after exercise is a diagnostic criterion for EIB. Anomalies in VE vs VCO₂ slope and PETCO₂ indicate impaired ventilation and perfusion in the pulmonary vascular bed, which may be related to pulmonary vasculopathies. The pulmonary perfusion to ventilation mismatching results in the increase in VE/VCO₂ and hypoxemia, i.e. reduction in SpO₂ is observed (see Chapter Pulmonary hypertension).

VE/MVV, FEV1 and PEF disorders occur in patients with a pulmonary cause of dyspnoea. Ventilatory limitations in exercise tolerance are usually diagnosed in the event of reduction in BR < 15-20%. In an isolated lung disease, VO₂peak is lower due to limited ventilatory capacity. This may also cause a reduction in HR peak. AT may be normal when the patient reaches the required level of exercise. In lung diseases, both of obstructive and of restrictive nature, a characteristic course of the VT vs VE and of the VE/VCO₂ relationship curves is observed.

Cardiovascular diseases are characterised by compromised ability to supply oxygen in response to the demand. VO₂peak and VO₂-AT, as well as the ratio of oxygen consumption to
the work performed (Δ VO₂/Δ WR) are reduced. O₂pulse values, representing indirect measurements of the stroke volume, are lower.

Table 5 presents CPET parameters useful in differentiation between cardiac and pulmonary causes of exertional dyspnoea.

The response of the above-mentioned parameters to exercise is not always unambiguous. When cardiovascular and lung diseases concur, the dominant cause of dyspnoea can be indicated only when the clinical context is taken into account.

<4>CPET in differentiation of exertional dyspnoea – conclusions

1 Indications: exertional dyspnoea, differentiation between cardiac and respiratory causes.

2 Main parameters: VE vs VCO₂ slope, % VO₂pred, PETCO₂ and BR.

3 Notes: spirometry at rest should be performed before CPET. SpO₂ monitoring during the test is recommended.

<3>Heart failure Heart failure is a complex pathophysiological process, in which haematological, metabolic, endocrine imbalance and sympathetic activation result from a defective heart function. CPET holds a well-established position and is a recommended test in heart failure patients. [34,41-50] According to the current European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and chronic heart failure, CPET [41]:

1 is recommended as a part of the evaluation for a heart transplantation and/or mechanical circulatory support (class I, C),

2 should be considered to optimise of exercise training (class IIa, C),

3 should be considered to identify the cause of unexplained dyspnoea (class IIa, C),

4 may be considered to detect reversible myocardial ischaemia (class IIb, C).
Individually selected protocols with gradually increasing workload are recommended (Naughton protocol, ramp-type protocols). CPET can be conducted on a treadmill or a bicycle ergometer.

Patients with advanced heart failure limit their daily physical activity, so they are very reluctant to undergo symptom-limited CPET. According to the latest guidelines, maximal CPET is understood as a test in which a patient reaches RER > 1.05 and achieves AT during the optimum pharmacotherapy (class I, B).[42] However, not all heart failure patients are able to achieve the optimal RER during symptom-limited CPET. It is caused by skeletal muscle disorders (morphological, structural, functional and metabolic), fatigue of respiratory muscles leading to abnormal ventilation, adverse effects of medications, or significant fatigue preventing continuation of the test.[43,44]

**Evaluation of heart failure progress** Traditional evaluation of heart failure progress is based on the Weber classification presented in Table 4.[7] Increasingly often parameters describing ventilation effectiveness (VE vs VCO₂ slope, PETCO₂, EOV) are also used to assess heart failure progress.[5] The ventilatory classification is shown in Table 5.[51]

**Prognosis in heart failure** CPET for evaluation of prognosis is performed at least one month after an episode of acute decompensated heart failure in patients in the stable clinical condition with established pharmacotherapy, which is defined as the lack of changes in the NYHA class and treatment, and no need for hospitalisation during the last 4 weeks.[43,44] There are indications that the patient’s ability to perform the test can itself be considered an predictor of a better prognosis.[43] According to the published data, patients with low VO₂peak (≤ 10 ml/kg/min) and RER ≥ 1.15 have the worst prognosis.

**CPET-based risk stratification algorithms in heart failure** The Committee on Exercise Physiology and Training of the Heart Failure Association of the European Society of
Cardiology published a proposal for CPET-based risk stratification for patients with heart failure.[43] The patients were divided according to “non-standard” or “standard” criteria of a referral for the test. The “non-standard” group, requiring individual specialised interpretation of results, included patients over 70 years of age, women, patients with atrial fibrillation or comorbidities affecting exercise tolerance, patients with an implanted left ventricular assist device (LVAD), patients who could only perform submaximal CPET (i.e. achieved RER < 1.0), patients with indications for end point evaluation or serial CPETs (a repeated test is suggested in patients with peak oxygen uptake < 14 ml/kg/min and in the case of disproportion between patient symptoms and results of other tests).

The “standard” group included all other patients with heart failure with a reduced left ventricular ejection fraction. The algorithm for CPET risk assessment in this group of patients is shown in Figure 2. When EOV occurs during the test, the risk is increased by one level in all patient subgroups.

Risk assessment in patients with HFpEF was based on % VO$_2$pred. Patients who achieved VO$_2$pred below 50%, have a risk that is mild to moderate, the remaining patients with ≥ 50% VO$_2$pred were included in the group with a very low risk.[43,44,48-50]

Certain CPET parameters were included as multiparameter prognostic factors developed for patients with chronic heart failure. For example, the MECKI score is based on % VO$_2$pred and VE vs VCO$_2$ slope, as well as other values.[45]

**<4>CPET in patients with chronic heart failure – conclusions**

1. Indications: evaluation of CHF stage (qualification for a heart transplantation and/or mechanical circulatory support), optimization of exercise training programme, evaluation of dyspnoea of unspecified origin, evaluation of ischaemia.
Main parameters: VO₂peak (at RER >1.05), % VO₂pred, VO₂ at AT, VE vs VCO₂ slope, PETCO₂, EOV, degree of HR decrease during rest, arrhythmias, blood pressure.

<3>Adults with congenital heart diseases

CPET is a necessary parameter for monitoring adult patients with congenital heart disease (ACHD). The main evaluated parameters include: VO₂peak, ventilation efficiency (VE vs VCO₂ slope), chronotropic response, heart rate disorders provoked by physical exercise, and blood pressure response to exercise. CPET result (as well as VO₂peak) is correlated with a number of hospitalisations and with the mortality rate in each ACHD.[52] Regularly repeated CPET helps to make a decision on the necessity and timing of potential intervention.

CPET in ACHD patients can be performed on a bicycle ergometer or on a treadmill.[53-55] During the test, close monitoring of electrocardiogram is necessary due to a frequent occurrence of arrhythmias, particularly in patients with tetralogy of Fallot (ToF) and in patients with transposition of the great arteries (TGA). When evaluation of the myocardial ischaemia is necessary (e.g. in aortic stenosis, coronary artery anomalies), a test on bicycle ergometer is preferred, due to a lower number of movement artefacts in the electrocardiogram. Blood pressure measurements during the test are particularly important in patients with aortic coarctation or arterial stenosis. Monitoring of arterial blood oxygen saturation by pulse oximetry throughout the test is also recommended (also during the initial stage, for assessment of initial saturation). In patients with cyanotic defects or with pulmonary hypertension, pulse oximetry ensures safe performance of the test.

For assessment of patients with ACHD, ramp-type and customised protocols are recommended.[56-60]

<4>Indications for CPET in ACHD patients

Indications for CPET in ACHD include:

1) the need for precise and reliable evaluation of exercise tolerance in ACHD patients as part of regular evaluation in specialised health care centres. This concerns in particular patients
post repair procedures (rToF, TGA, patients status post Fontan procedure) and with Eisenmenger’s syndrome [61];

2) initial symptom evaluation (e.g. in patients with bicuspid aortic valve and aortic valve stenosis, or who underwent surgery for a heart defect as a child);

3) evaluation of chronotropism, presence of atrioventricular blocks before pacemaker implantation;

4) evaluation of pharmacotherapy;

5) evaluation of cardiac rehabilitation results;

6) evaluation of surgery results.

<4> Contraindications to CPET in ACHD patients Contraindications do not differ from those specified for electrocardiographic exercise testing. Additionally, the following should be considered (as relative contraindications):

1) severe aortic/pulmonary/mitral stenosis;

2) significant right or left ventricular outflow tract obstruction;

3) arterial anomalies requiring surgical treatment;

4) severe pulmonary hypertension.

<4> The most important CPET parameters in ACHD patients VO2peak is the best individual indicator for exercise tolerance, risk of hospitalisation and death. Women accomplish 65-75% of VO2peak achieved by men (excluding patients with Eisenmenger’s syndrome).[62] The lowest VO2peak values are observed in patients with Eisenmenger’s syndrome, with cyanotic heart defects, after Fontan procedure, with corrected TGA (with accompanying defects, e.g. ventricular septal defect and pulmonary valve stenosis) or with
TGA after physiological corrections, e.g. after Mustard/Senning repair. The highest VO2peak is observed in patients with TGA after anatomical correction, in patients with valvular defects, and after surgical repair of aortic coarctation. Patients with cyanotic heart defects have the worst exercise tolerance amongst all patients with ACHD.[63]

VE vs VCO2 slope is the best mortality predictor in non-cyanotic patients.[64] The highest values are observed in PH patients in the course of congenital heart disease, with complex heart defects, with cyanotic heart defects with right to left shunt., and the lowest in patients with TGA after anatomical correction and in CoA patients.[64,65]

AT is frequently not achieved in patients with cyanotic heart defects, with complex heart defects and with the weakening of skeletal muscles.

HR reserve depends on the exercise level. It is an independent predictor of death in ACHD patients, also in patients treated with negative chronotropic medications.[65]

The analysis of the most important CPET parameters in the selected congenital heart diseases in adults is shown in Table 8.

<4>Application of CPET in selected ACHD  Patients with ACHD, due to long-term adaptation to the disease, even when asymptomatic, can have significantly lowered VO2peak. In these patients, many factors contribute to the aetiology of lower exercise tolerance. Patients with simple non-cyanotic defects not accompanied by pulmonary hypertension have higher exercise tolerance than patients with complex cyanotic defects or with pulmonary hypertension. CPET results allows making a decision about modifying pharmacotherapy and determining timing of cardiac intervention especially in patients with ToF after surgical correction, Ebstein’s anomaly or after Fontan procedure. In patients with repaired ToF, significant pulmonary valve insufficiency develops in the course of the disease, as well as dilation and impaired function of the right ventricle. Reduced VO2peak indicates lack of
cardiac and circulatory reserves to adequately increase stroke volume during exercise. The accompanying deterioration in the right ventricular function in echocardiography supports a decision of pulmonary valve replacement. CPET is also a well established tool for monitoring patients with a pulmonary valve dysfunction in many heart defects after percutaneous pulmonary valve implantation.\[^{66}\] Reduced exercise tolerance recorded in CPET in patients with Ebstein's anomaly and significant tricuspid valve insufficiency is a generally recognised indication for a valve repair (recommendation class IC according to ESC).\[^{61,67}\]

The range of normal values to be used for CPET results interpretation in ACHD patients remains a controversy. It is not recommended to compare the exercise capacity of patients with ACHD to that of healthy people, as in this group of patients exercise tolerance differs depending on the heart defect type or even on the repair procedure performed. Patients with TGA post physiological repair procedures can serve as an example here, as their capacity is significantly lower than that of TGA patients post anatomical corrections. Another example are patients post Fontan procedure who, depending on the operation method (standard surgery – aortopulmonary collaterals (APC) versus total cavopulmonary connection (TCPC)) can have a entirely different exercise capacity. The best solution to this problem would be individual databases with reference values for particular heart defects created by each centre providing care to ACHD patients.\[^{63}\]

**<4>CPET in patients with ACHD – conclusions**

1. Indications: an objective assessment of exercise tolerance in patients status post repair procedures, evaluation of symptoms related to exercise, evaluation of chronotropic response, evaluation of pharmacotherapy and/or surgery outcomes, and evaluation of the rehabilitation progress.

2. Main parameters: \( VO_{2\text{peak}} \), VE vs \( VCO_{2} \) slope, chronotropic response, HR reserve, arrhythmias, and blood pressure.
**Hypertrophic cardiomyopathy**

AHA recommendations regarding exercise stress tests list hypertrophic cardiomyopathy (HCM) with left ventricular outflow tract obstruction (LVOTO) and significant gradient as a relative contraindication to an exercise stress test. [3] However, the recent data suggest that exercise stress tests in HCM patients are not only safe, but can also be an important part of a comprehensive evaluation.[68,69] CPET, according to ESC guidelines, is recommended to evaluate the progression and mechanism of exercise tolerance, and to evaluate changes in SBP during exercise (class IIa, evidence level B).[70] CPET does not replace stress echocardiography, but is its valuable supplement.[71]

**Electrocardiographic evaluation during exercise**

In an electrocardiogram of HCM patients, the most commonly observed are signs of left ventricular hypertrophy with ST segment depression and pathological Q waves. In an apical HCM, deep inverted T waves are observed in precordial leads. In many HCM patients, conduction disturbances, especially LBBB are observed.[72] The presence of changes described above prevents reliable evaluation of ischaemia during exercise. In 45% of HCM patients, arrhythmia may occur during exercise: atrial fibrillation in 2%, nonsustained ventricular tachycardia in 1.2%, and single ventricular ectopic beats in 33%.[73]

**Blood pressure profile evaluation**

Four types of blood pressure response to exercise can be observed in HCM patients:

1. hypotensive response with a continuous drop in SBP from the start of exercise,
2. hypotensive response in the form of a sudden drop in SBP from the maximum value,
3. normal SBP response during exercise, but an initial rapid drop at the early stage of recovery, and then a gradual increase by 10 mmHg from the minimum value,
4. normal blood pressure response to exercise.

Inadequate blood pressure response to exercise in HCM is usually defined as SBP drop or increase by < 20 mmHg versus initial values and is observed in 20% to 40% of patients.
Abnormal blood pressure response provides prognostic information and is considered to be one of the markers for the risk of death in HCM patients.[74-77] Inadequate blood pressure response to exercise has low positive and high negative predictive value, thus it is the most useful for identification of patients with a lower risk of death.[75] Therefore, patients with an abnormal blood pressure response require other additional tests to stratify the risk of death.

**Differential diagnosis** CPET is a useful supplementary tool in differentiation of HCM and “athlete’s heart”, especially in cases of unclear echocardiographic images (“grey zone” wall thickness). In HCM patients, a reduction in VO$_2$-peak and in VO$_2$-AT is to be expected, but in people with athlete’s heart VO$_2$-peak should reach values of > 50 ml/kg/min (or > 20% above the predicted value).[78]

**Prognostic value** Numerous studies demonstrated that VO$_2$-peak is correlated with many clinically significant variables, i.e. degree of diastolic dysfunction or quality of life.[79,80] Furthermore, a reverse correlation with the pressure gradient in the left ventricular outflow tract was also identified, while myectomy and alcohol ablation procedures aiming at reduction in the LVOTO cause an increase in VO$_2$-peak.[81,82] In the study conducted at Mayo Clinic and on a group of 182 HCM patients with LVOTO, with or without mild symptoms, lower % VO$_2$-pred values were associated with a higher risk of a composite endpoint defined as a all-cause mortality rate and progression to advanced heart failure.[83]

It was proven several times that low VO$_2$-peak is an independent predictor of serious adverse events in HCM.[68,69] In another large study involving 1898 HCM patients (62% with LVOTO), VO$_2$-peak, VO$_2$-AT and VE vs VCO$_2$-slope were predictors of all cause mortality and heart transplantation.[84].

As a part of the eligibility process, it is considered that a value of VO$_2$-peak $\leq14$ ml/kg/min (or < 50% VO$_2$-pred) is a one of the criteria for a heart transplantation.[85] CPET is recommended
in patients with severe clinical symptoms, left ventricular systolic and/or diastolic dysfunction as part of evaluation for heart transplantation or for the left ventricular assist device implantation (class I, evidence level B).[70]

<4> Qualification for alcohol ablation and myectomy

According to ESC guidelines, CPET should be considered in symptomatic patients who are candidates to septal myectomy or alcohol ablation to evaluate exercise tolerance (class IIa, evidence level C).[70] No data is available indicating specific values for VO\textsubscript{2}peak, supporting a decision for earlier myectomy or alcohol ablation in LVOTO patients with mild symptoms, or delaying the procedure in patients with significant LVOTO but normal values of CPET parameters.[86]

<4> Follow-up and risk stratification

CPET can provide objective evidence for disease progression, but the frequency of performance of the follow-up CPET is not extensively supported by scientific evidence, and according to ESC guidelines this test can be considered every 2 to 3 years in patients in a stable clinical condition or every year in patients whose symptoms are progressive (class IIb, evidence level C).[70]

There are several risk models described in the literature which are based on echocardiography and CPET. In the HYPertrophic Exercise-derived Risk HF (HYPERHF) model for evaluation of a composite endpoint (death due to heart failure, heart transplantation, progression of heart failure to NYHA class III-IV, exacerbation of heart failure requiring hospitalisation, septal myectomy and alcohol ablation procedures), the peak circulatory power (a product of VO\textsubscript{2}peak and peak SBP), VE vs VCO\textsubscript{2} slope, and left atrium dimension (in parasternal long axis view) were independently related to the composite endpoint.[69]
Finocchiaro et al. demonstrated that reduced physical capacity (<80% VO\textsubscript{2}pred), VE vs VCO\textsubscript{2} slope > 34 and the left atrial volume index > 40 ml/m\textsuperscript{2} were independent predictors of the composite endpoint (procedures of intraventricular septum reduction, heart transplant and cardiac death).[87] Similarly, in a large study involving 1005 HCM patients, lower absolute and percentage predicted VO\textsubscript{2}peak, inadequate chronotropic response, and a lower left ventricular ejection fraction were independent predictors of the composite endpoint (adequate discharges of a cardioverter-defibrillator, resuscitation, stroke, heart failure, and death).[68]

**CPET in patients with HCM - conclusions**

1. Indications: to evaluate progression and mechanism of exercise intolerance, to evaluate changes in SBP during exercise.

2. Main parameters: VO\textsubscript{2}peak, % VO\textsubscript{2}pred, VE vs VCO\textsubscript{2} slope, PETCO\textsubscript{2}, SBP, arrhythmias, ST-T changes.

1.1. *Pulmonary hypertension*

CPET is performed in patients with pulmonary hypertension (PH) in evaluation of disease progression, presence of patent foramen ovale with right-left shunt, and evaluation of prognosis, treatment response, and indications for heart and lung transplant.[5,25,27,88-90] Contraindications to CPET include syncope, significant arrhythmia, and acute right ventricular heart failure.

In patients with pulmonary arterial hypertension (PAH), ESC proposed complex prognostic evaluation, which includes two CPET parameters: VO\textsubscript{2}peak and VE vs VCO\textsubscript{2} slope.[89]

In patients with PH, both primary and secondary, the evaluation of VO\textsubscript{2}peak, VE vs VCO\textsubscript{2} slope and and PETCO\textsubscript{2} during exercise is useful, as changes in these parameters are related to mismatch between pulmonary perfusion and ventilation.[88]
Changes in VE/VCO$_2$ and PETCO$_2$ will be different in PAH patients, when compared to patients with PH caused by left heart disease or related to lung diseases and/or hypoxia. These parameters are used as the basis for differential diagnosis of clinical groups (aetiologies) of pulmonary hypertension.[91]

CPET result in PH patients is characterised by low PETCO$_2$, high VE vs VCO$_2$ slope, low O$_2$ pulse, and low peakVO$_2$.[92] Regardless of the clinical group of pulmonary hypertension, VO$_2$ peak is reduced proportionally to the disease severity, depends on the level of pulmonary vascular resistance and reduced stroke volume. In young people, %VO$_2$pred appears to be more appropriate, and in this respect CPET has an advantage over the 6 minute walk test. On the basis of high VE vs VCO$_2$ slope or VE/VCO$_2$ values, and low PETCO$_2$ values (decreasing during exercise), conclusions can be drawn on the progress of anomalies in the haemodynamic parameters of pulmonary circulation and a poor prognosis for patients.[91]

In many patients with PAH, chronic thromboembolic pulmonary hypertension and PH associated with lung disease/hypoxia, SpO$_2$ drops during CPET. Table 9 presents changes in ventilation parameters in PAH.

In PAH patients, CPET can reveal the presence of a right-left shunt on the atrial level, as a consequence of a right atrial pressure increase exceeding left atrial pressure during exercise. The criteria for shunt diagnosis include low PETCO$_2$ at rest, with a drop at the beginning of exercise with a simultaneous sudden increase in PETO$_2$, VE/O$_2$ and RER, and with an accompanying drop in SpO$_2$.

CPET is recommended for a periodic assessment of PAH patients every 6 to 12 months, and additionally, in case of clinical exacerbation.[89] Table 10 depicts the use of CPET parameters for the evaluation of one year mortality risk in PAH.

<4>CPET in pulmonary hypertension - conclusions
1 Indications: evaluation of disease progression, presence of patent foramen ovale with the right-left shunt, and the evaluation of prognosis, treatment results, and indications for heart and lung transplants.

2 Main parameters: VO$_2$peak, VE vs VCO$_2$ slope, % VO$_2$pred, PETCO$_2$.SpO$_2$,SBP, arrhythmias.

Coronary artery disease CPET improves diagnostic, prognostic and monitoring possibilities of the electrocardiographic exercise test in coronary artery disease (CAD).[93,94] CPET sensitivity and specificity in CAD diagnostics are higher than the electrocardiographic exercise test (87% vs 46% and 74% vs 66%, respectively), and this enables diagnosis in patients who previously had electrocardiographic exercise test determined as negative.[93] The main CPET advantage over other diagnostic methods used to diagnose CAD is the possibility to find and evaluate quantitatively functional haemodynamic disturbances induced by ischaemia.[95,96] In a cascade of ischaemic changes caused by progressively increasing exercise, these haemodynamic disturbances precede electrocardiographic (ST depression/elevation) and clinical (chest pain) signs of ischaemia. This is of particular clinical importance for the identification of the early stages of ischaemic heart disease without significant coronary stenosis.[97] This clinical form of CAD, symptomatic or presenting as atypical picture, affects women more frequently than men, and is characterised by an increased risk of acute coronary syndromes.[98] Its early diagnosis enables the initiation of complex management including reduction of modifiable risk and pharmacotherapy.

Haemodynamic and electrocardiographic anomalies secondary to ischaemia are analysed in CPET on the basis of [5,93-97]:

1 trend in O$_2$ pulse vs WR: course of the O$_2$pulse curve in relation to WR.

2 trend in VO$_2$ vs WR: course of the VO$_2$ curve in relation to WR.
haemodynamic response to exercise: (trend HR vs WR: course of the HR curve in relation to WR, SBP),
relative capacity (% VO$_2$pred),
electrocardiographic evaluation,
reason for test termination.

O$_2$ pulse and VO$_2$ are parameters reflecting SV and cardiac output. The course of O$_2$ pulse trend vs WR, of a straight-line character in healthy people, is flattened (plateau) or even reduced when systolic dysfunction occurs due to cardiac ischaemia. Figure 3 shows schematic normal and pathological courses of O$_2$ pulse vs WR.

In normal conditions, the straight-line HR growth rate is observed in relation to the increasing load. In subjects with a normal chronotropic response to exercise and ischaemia induced by exercise with an accompanying drop in SV, a compensating higher HR increase occurs when compared during the initial period of exercise, below ventilation threshold VT1. A schematic course of HR and O$_2$ pulse trends in relation to the load is shown in Figure 4.

In patients with impaired chronotropic response to exercise due to pathological or iatrogenic causes, the impaired stroke volume resulting from cardiac ischaemia induced by exercise is manifested as a clearly disrupted course of the VO$_2$ vs WR curve, analogically as the O$_2$ pulse vs WR trend (Figure 5).

In the final CPET report, a character of the O$_2$ pulse vs WR and VO$_2$ vs WR trends must be described as: ongoing increase with a rising load; early, maintained plateau; early plateau and a reduction during exercise.

Relative capacity, calculated as % VO$_2$pred, relates to ischaemic disease progression, although it is not a specific parameter. % VO$_2$pred values in successively repeated CPET have a great prognostic importance, also confirming effectiveness of the treatment.
Table 11 shows diagnostic stratification for patients with suspected myocardial ischaemia based on CPET.[5,96,97]

<4>CPET in coronary artery disease - conclusions

1 Indications: diagnostics of ischaemia.
2 Main parameters: O₂ pulse vs WR trend, VO₂ vs WR trend, HR vs WR trend, SBP, % VO₂pred, changes in ST-T, arrhythmias, reason for test termination (lower extremity muscle fatigue, angina, dyspnoea).

<3>Patients with implantable devices A scope of CPET application increasingly expands, to include the evaluation of patients with implantable devices (CIED): pacemakers, cardioverter-defibrillators (ICD), and cardiac resynchronization devices (CRT). The most common CPET application in patients with CIEDs is patient evaluation before and after CRT implantation, evaluation of chronotropic capacity and optimisation of stimulation thresholds. The most important CPET parameters in patients with CIEDs are: VO₂peak, ventilation efficiency (VE vs VCO₂ slope), chronotropic response (particularly in heart failure patients), stimulation effectiveness evaluation during exercise (important in patients with CRT) and heart rhythm disorders caused by exercise.

<4>Test methods and protocol selection In patients with CIED, a preferred method is the test on a treadmill, due to higher VO₂peak obtained in the treadmill test, and a better chronotropic response in patients with a rate-responsive function activated.[53,54,100] The evaluation of myocardial ischaemia in an electrocardiogram is difficult in patients with a stimulated ventricular rhythm. The same load protocols are applied as in patients without CIEDs. In patients with CRT, protocols used for the evaluation of patients with heart failure are preferred.[56] Before a patient with CIED undergoes a test, it is necessary to determine the device settings, especially its base stimulation rate, maximum tracking rate (MTR), atrioventricular delay (AV delay), thresholds for detecting arrhythmias in patients with ICD.
and CRT-D (so-called VT/VF detection zones), and a programmed algorithm for VT/VF termination with antitachycardia pacing or defibrillation. The target HR during exercise should be 10-20 bpm lower than the arrhythmia detection threshold. The device can also be reprogrammed, e.g. with therapy deactivated in the VT zone, by increasing VF > 220 bpm detection threshold, or by increasing arrhythmia detection threshold above maximum HR.[27] In this situation, the presence of a person programming the device is required during the test. In pacemaker dependent patients and in patients with CRT, attention should be paid to the HR value at which 1:1 conduction is maintained. Exceeding this value may cause a sudden slowing of the frequency of the stimulated ventricular rhythm, a drop in stroke volume, and haemodynamic symptoms. The frequent occurrence of such symptoms requires the reprogramming of the device, particularly, in young patients with good physical exercise tolerance, in whom an increase in the maximum tracking rate (MTR) is recommended.[101]

<4> Indications and contraindications to CPET in patients with CIEDs

Indications for CPET in patients with CIEDs include: 1) evaluation before CRT implantation and evaluation of the response to CRT, 2) evaluation of the chronotropic response and settings of the rate-responsive pacing, 3) optimisation of atrioventricular delay in patients with sequential stimulation, 4) evaluation prior to rehabilitation and qualification for training, 5) evaluation of rehabilitation results.

Absolute contraindications include: haemodynamically significant arrhythmias, electrical storm, pacing and sensing disturbances.

<4> Current and potential CPET applications in patients with CIEDs

CPET, as a reference method for the evaluation of heart failure patients, is used to qualify patients for CRT and in an objective evaluation of the resynchronization therapy.[102,103] VO$_2$peak improvement is commonly accepted as one of the criteria of response to CRT.[104-}
The volume of data indicating that initial $\text{VO}_2\text{peak}$ might predict a response to CRT is increasing [107-110].

CPET is also used for the optimisation of stimulation programmes (e.g. a reduction in excessive stimulation by elongating the AV interval) and in the selection of an appropriate simulating programme for patients with chronotropic incompetence.[111,112] Chronotropic incompetence, frequently occurring in CHF patients, limits exercise tolerance and can be reduced by the appropriate programming of the device, and evaluation with CPET is useful in that respect.[113-115]

However, further multicentre studies on CPET role in patients with CIEDs, especially with CRT, are necessary, to establish the role of that test in the group of patients with implantable devices.

**<4>CPET in patients with CIEDs - conclusions**

1. **Indications**: patient evaluation before and after CRT implantation, evaluation of chronotropic capacity and optimisation of stimulation thresholds, evaluation before planned rehabilitation.
2. **Main parameters**: $\text{VO}_2\text{peak}$, $\text{VE vs VCO}_2$ slope, chronotropic response, stimulation effectiveness during exercise, arrhythmias caused by exercise.
3. **Notes**: before starting the test, it is necessary to become acquainted with the implanted device.

**<3>Chronic pulmonary diseases**  CPET is a useful tool in evaluation of respiratory diseases. Its performance is especially warranted in the case of symptoms related to exercise. CPET should be considered in the following clinical scenarios: exertional dyspnoea, concurrent pulmonary and non-pulmonary causes of exertional dyspnoea, subclinical forms of pulmonary disorders, when basic diagnostic methods do not result in an unambiguous
diagnosis, or prognosis assessment in chronic disorders.[116,117] Each CPET should be preceded by spirometry at rest, which is one of the basic diagnostic tools in respiratory disorders.

**Obstructive lung diseases - CPET diagnostic value** In accordance with the recommendations of the Global Initiative for Asthma (GINA), bronchial asthma can be diagnosed on the basis of spirometry at rest, when the FEV1/FVC ratio drops below 0.75–0.8 of the predicted values.[116] The guidelines of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) specify the FEV1/FVC value below 0.70 after inhalation of bronchodilator as a cut-off value for COPD diagnosis.[117] CPET may prove to be an indispensable tool in the case of exercise-induced bronchial obstruction. To document its occurrence, it is recommended to record the flow-volume loop before exercise, at its peak and during the post-exercise phase.[26,118-120] Diseases accompanied by bronchial obstruction change the shape of this curve (Figure 6).

CPET also enables the evaluation of mechanisms underlying exertional dyspnoea. An increase in VE vs VCO\(_2\) slope and VE/VCO\(_2\) nadir indicates that the physiological dead space volume is enlarged, while an abnormal shape of the flow-volume curve reflects the magnitude of exertional obstruction. Low (<20% of predicted value) BR value at the peak exercise may suggest a ventilation-related cause of reduced exercise tolerance.[121]

**Obstructive lung diseases - CPET prognostic value** In COPD, the prognostic value was proven for VE vs VCO\(_2\) slope (poorer 4-year prognosis for the result > 30.0, with subsequent cut-off points for 35.9 and 44.9), PETCO\(_2\) (poorer prognosis for the at rest value <33.0 mmHg and the exercise-related increase <3mmHg), and for VO\(_2\)peak (poorer prognosis in Weber classes >A).[5] VO\(_2\)peak can be taken into account if exercise was terminated with RER>1.0 or due to electrocardiographic abnormalities or pathological haemodynamic response.[26]
Restrictive lung disease - CPET diagnostic value

CPET changes specific for restrictive lung diseases are: lower VO₂peak and an increase in parameters related to the enlarged physiological dead space. As similar anomalies can also occur in obstructive disease, spirometry at rest and the flow-volume loop during and after exercise should also be evaluated. BR evaluation may also be useful (usually > 50% at peak exercise in restrictive disorders).[32]

Restrictive lung disease - CPET prognostic value

CPET parameters used in prognostic evaluation are analogous to those used in obstructive lung diseases.[26,122]

Chest wall pathologies

Patients with disorders affecting the chest wall such as chest deformations, muscle disorders, and severe obesity present a reduced VO₂peak. CPET allows to establish whether exertional dyspnoea is masking comorbidities, and this is of particular importance for obese people. Chest wall disorders as a basic mechanism of exertional dyspnoea may be suspected in the case of high BF accompanied by their low volume and a high VT/IC ratio.[40]

Preoperative evaluation

In the case of patients with planned pulmonectomy or lobectomy, values VO₂peak > 15 ml/kg/min are associated with a better prognosis, even in patients with worse lung function in spirometry. The values <10 ml/kg/min are associated with a poorer prognosis.[25,123,124] Prognosis is also negatively affected by exercise-related abnormalities in the electrocardiogram and by specified symptoms of coronary artery disease.[26]

CPET in chronic lung diseases - conclusions
1 Indications: exertional dyspnoea, suspected exertional obstruction, subclinical forms of pulmonary disorders, prognosis evaluation in chronic diseases, preoperative evaluation.

2 Main parameters: VO$_2$peak, VE vs VCO$_2$ slope, PETCO$_2$, BR, SpO$_2$, and a flow-volume loop.

3 Note: exercise testing should be preceded by resting spirometry, EIB may also occur after cessation of exercise.

**<3>Clinical oncology**

This subchapter discusses the role of CPET in patient evaluation during oncologic treatment or follow-up in cancer survivors. Risk stratification with the CPET before surgeries in cancer patients was discussed in chapter Pre- and post-operative assessment.

**<4>Differential diagnostics of dyspnoea in oncology**

Cardiopulmonary capacity, and thus patient functional performance, belong to the most important clinical criteria for cancer treatment eligibility. An objective evaluation can be difficult in some special populations, such as elderly people, patients with obesity or metabolic disorders, cancer disease of the respiratory system, and abnormal echocardiography results before they are qualified for potentially cardiotoxic chemotherapy.[125-127] CPET is recommended in cancer patients, because it enables an objective evaluation of their physical capacity (VO$_2$peak measurements) and differential evaluation of comorbidities limiting exercise capacity.[128] This test remains reliable, regardless of the patient’s motivation to make the maximum effort and this may be of importance in patients with depression, which is common in oncology patients. Considering that a large percentage of cancer patients have at least one important comorbidity, often cardiovascular, CPET becomes a valuable tool for the objective evaluation of functional performance prior to cancer therapy.[129] The usefulness of VO$_2$peak measurement in oncology was proven in many clinical situations.[130,131] The
evaluation of ventilation parameters, such as VE, VT and BF, is particularly useful in patients with lung cancer, advanced cancer with lungs metastases, and with lung comorbidities.

**Evaluation during or after anticancer therapy**

Cancer therapy (radiotherapy, chemotherapy, molecularly targeted therapy, immunotherapy) and supportive treatment used in oncology (e.g. glucocorticoids) may cause heart perfusion anomalies, symptomatic or asymptomatic decrease of left ventricular ejection volume, as well as anaemia, autonomic dysfunction, lung fibrosis, pulmonary dysfunctions, endothelial dysfunction, and myopathies.[132-141] In consequence, cancer treatment, both previous, and current, in combination with cancer disease progression, particularly at the metastatic stage, negatively affects aerobic metabolism during exercise by changing the activity and number of red blood cells (anaemia), disrupting lung diffusion (damaged alveolar-capillary barrier in lungs), deteriorating ventilation response during exercise, causing changes in oxygen transport (changes in the function of capillaries), and disrupting the respiratory chain (mitochondrial damage).[142]

One of the most important problems in modern clinical oncology is cancer-related fatigue (CRF), associated with cancer disease itself, and with its treatment. One of the meta-analyses establishes the influence of various forms of recommended exercise during cancer therapy on the subjective feeling of fatigue.[143] Eighteen studies with randomisation (12 on breast cancer, 4 on prostate cancer, 2 on other cancers) were analysed. In patients with breast cancer, only controlled aerobic exercise led to a significant reduction in CRF. Another meta-analysis focused on whether physical activity is appropriate and effective in patients during and after cancer therapy.[144] After analysing 82 studies, it was demonstrated that physical activity is advantageous for muscle strength, symptoms of fatigue, self-esteem, anxiety, functional condition, and quality of life. CPET seems to be an ideal test for the objective evaluation of the sense of fatigue related to cancer treatment, as well as for excluding the progress of
concurrent heart failure and encouraging the patient to initiate physical training, even as a form of recreation.

Patients who underwent cancer therapy have lower physical capacity, which, to some extent, must be associated with adverse effects of chemo- and radiotherapy.[145] Even athletes have significant changes in VO$_2$-AT during exercise after chemotherapy for Hodgkin lymphoma.[146] CPET can, in a simple way, demonstrate a significant difference in deterioration in physical capacity between healthy people and patients who underwent cancer therapy.[147,148]

People who underwent cancer therapy in childhood experience premature complications of cardiovascular and other systems (respiratory, neuroendocrine, etc.), which may significantly reduce their physical capacity.[149] In an age-independent analysis it was demonstrated that VO$_2$peak is lower in these patients, when compared to healthy peers: in men: 28.53 vs 30.90 ml/kg/min (p=0.08), and in women 19.81 vs 23.40 ml/kg/min (p=0.03). Furthermore, in men older age (p=0.01), higher content of fat (p<0.001), high or low left ventricular mass (p=0.03) predicted lower VO$_2$peak, while in women lower VO$_2$peak was indicated by older age (p<0.001), methotrexate treatment (p=0.01), and left ventricular contractility abnormalities (p=0.02). In conclusion it was stated that this group of patients should be covered by regular, well-planned training with appropriate monitoring.

Similarly, young adults who undergone therapy for acute lymphoblastic leukaemia (ALL) are at a higher risk of delayed cardiotoxicity caused by anthracyclines.[150] It was demonstrated that reduced VO$_2$peak [ml/kg/min] might affect 47% of patients, more often in those post anthracycline therapy than those undergoing other regimens (56% vs 17%, p<0.001). In a multivariate analysis, anthracycline therapy was negatively correlated with VO$_2$peak [ml/kg/min], while in echocardiography, parameter e’ was the best predictor for VO$_2$peak [ml/kg/min]. In the conclusion it was emphasised that myocardial contractile dysfunction was
correlated with exercise intolerance, particularly, in patients previously treated with anthracyclines.

Evaluation of training results in cancer patients

ESC Position Paper indicates aerobic physical exercise as a promising non-pharmacological strategy for the prevention and/or treatment of chemotherapy-induced cardiotoxicity.[151] The listed results included improved cardiopulmonary capacity and cardiovascular function and an increase in the percentage of patients continuing chemotherapy until its planned end, reduced frequency and intensity of adverse effects, such as nausea, fatigability, and pain.

There is an increasing need for a practical use of CPET in cancer patients to plan their physical training.[152-154] Initial CPET not only allows to establish exercise capacity and optimally plan the training intensity, but most importantly, identifies people with contraindications to physical exercise.[155]

Increasingly more cancer patients want to remain physically active both during cancer treatment and after its completion.[156,157] Following an appropriate training plan and maintaining the patient’s physical activity, a normal CPET result can be maintained in these patients, regardless of electrocardiographic and echocardiographic anomalies, even in lung cancer patients, in whom underlying disease reduced lung capacity during exercise.[158,159] Conducting training based on HR at AT, after 8–12 weeks, a 10–12% improvement in VO$_2$peak can be achieved both in healthy people and in patients post cancer therapy.[160] Breast cancer patients who train regularly during cancer therapy do not experience a drop in aerobic metabolism during exercise and maintain normal body weight during and post chemo-and radiotherap.[161] Even patients post bone marrow transplant, training on the basis of AT determined during CPET improve their ventilation capacity by ca. 28% and reduce their subjective sense of fatigue.[162]
**CPET in oncology - conclusions**

1. Indications: differential diagnostics of dyspnoea, evaluation during or after cancer treatment, qualification for cardiac rehabilitation and evaluation of its results, risk stratification before surgery.

2. Main parameters: VO$_2$-peak, VO$_2$-AT, VE, VT, BF.

**Pre- and post-operative assessment**  
A trend for the use of preoperative CPET to evaluate the risk of adverse perioperative events and to plan appropriate perioperative care in patients undergoing surgery is rising globally, particularly in the United Kingdom. However, in Poland the use of CPET for this purpose seems to be significantly limited.

The extensive literature data suggest the use of CPET to predict risk during major surgery, especially, major abdominal, colon, urological, liver and bile ducts, liver transplantation, vascular, and chest surgery.

[163-173] The importance of patient evaluation after neoadjuvant chemotherapy and radiotherapy preceding oncologic surgery has been demonstrated.

[174] CPET may also be useful in the selection of patients referred for rehabilitation to improve their capacity before or after surgery.

**Indications for preoperative CPET**  
Indications for preoperative CPET includes:

1. assessment of perioperative morbidity and mortality,

2. additional information supporting cross-disciplinary decision-making processes (e.g. organ transplant qualification procedures),

3. supporting decision-making to choose the best perioperative care (intensive care, high dependency care or a general ward),

4. to support a decision about possible preoperative interventions, i.e. expanded evaluation and treatment of comorbidities,
assessment of newly diagnosed comorbidities,
as a part of the qualification for pre- and postoperative rehabilitation programme,
to obtain additional information before deciding about the type of anaesthesia used for the surgery.

Contraindications to CPET

Contraindications to CPET are the same as in other populations (in accordance with ATS guidelines).[1] It should be noted that patients before vascular surgery can undergo CPET this test, as the abdominal aortic aneurysm of more than 8 cm in diameter is only a relative contraindication to exercise testing. Care should be taken in the case of cancer patients, due to thromboembolic complications common in this group. Although asymptomatic severe aortic stenosis is a relative contraindication to the exercise testing, CPET may help in a decision about an order of procedures in case of comorbidities.

Prognostic value of CPET

In the case of multiple operations, CPET allows the assessment of peri- and postoperative prognosis. However, unambiguous and final recommendations based on specific parameters cannot be made. The following CPET parameters of a prognostic value have been identified: VO2peak, VO2-AT, VE/VCO2 at AT. An attempt can be made to sum up and specify cut-off points for individual parameters for certain types of surgery:

1. liver transplantation: 90-day survival - VO2-AT 9 ml/kg/min; 3-year survival - VO2-AT 11.5 ml/kg/min; and admittance to an intensive care unit - VO2-AT <9.9-11 ml/kg/min;
2. vascular surgery for abdominal aortic aneurysm: 90-day survival - VO2peak 15 ml/kg/min;
3. pancreatic surgery: hospitalisation length - VO2-AT 10–10.1 ml/kg/min;
4. other surgeries within the abdominal cavity: mortality - VO2-AT 10.9 ml/kg/min.
Data from published studies on hospital, short- and long-term mortality, and hospitalisation length post-surgery is shown in Table S1.

**Key components of preoperative CPET interpretation** A test report should include parameters of a predictive value for peri- and postoperative risk, i.e. VO2peak, VO2-AT and VE vs VCO2 slope and VE/VCO2 at AT. The reason of limited exercise tolerance should be identified. It is also suggested to include in the report a conclusion about perioperative risk, as well as implications concerning further preoperative tests and interventions.

2014 ESC/ASA guidelines do not recommend a routine CPET assessment before non-cardiac surgery.[177] Nevertheless, it seems that CPET may be a valuable tool for perioperative risk stratification and for planning of postoperative care. Concluding, VO2-AT is an optimal predictor of prognosis for liver, pancreas and other abdominal surgeries, while for the abdominal aortic aneurysm, VO2peak remains the best prognostic parameter.

**CPET in pre- and postoperative evaluation - conclusions**

1. Indications: pre- and perioperative risk assessment, diagnosis of comorbidities, qualification for pre- and postoperative rehabilitation programmes.
2. Main parameters: VO2peak, % VO2pred, VO2-AT and VE vs VCO2 slope, VE/VCO2 at AT.

**Cardiac rehabilitation** According to WHO definition cardiac rehabilitation is the sum of activities required to provide the patients with the best possible physical, mental and social conditions so that the patients may, by their own efforts, preserve or resume as normal a place as possible in the community.[178] In recent decades, cardiac rehabilitation has evolved from traditional programmes based mainly around physical activity towards complex activities covering optimal pharmacotherapy and invasive treatment to reduce clinical symptoms and
improve prognosis, modification of cardiovascular risk factors, physical training, and education, together with psychological support, and social and occupational rehabilitation.

Aims for CPET performance in cardiac rehabilitation [26,27]:

1. gold standard in the evaluation of physical exercise tolerance; VO$_{2\text{max}}$ or VO$_{2\text{peak}}$ measurement, and VCO$_2$;
2. differential diagnostics of dyspnoea of unspecified origin;
3. demonstration of disease symptoms that do not occur at rest, including rhythm and conduction disturbances, myocardial ischaemia, etc.,
4. stratification of cardiovascular risk related to physical exercise,
5. determination of physical training intensity: loads and HR,
6. evaluation of cardiac rehabilitation results;
7. evaluation of prognosis;
8. for the needs of occupational therapy

An individual aerobic physical training plan is based on two methods:

a) VO$_2$-AT evaluation (*example: when a heart failure patient achieves VO$_2$peak of 16 ml/kg/min, and VO$_2$-AT 12 ml/kg/min at HR of 105 bpm during CPET with a load protocol ramp 10 W/min, then the recommended training HR will be ca. 105 bpm),

b) calculation of training VO$_2$ (T VO$_2$) on the basis of VO$_2$ reserve (VO$_2$ R), using an equation proposed by Karvonen et al. [179]

\[
T \text{ VO}_2 = (\text{VO}_2\text{max} - \text{VO}_2 \text{ rest}) \times (0.01 \times \text{training intensity as percentage*}) + \text{VO}_2 \text{ rest}
\]

* training intensity as percentage- 40 to 85% is recommended, depending on the cardiovascular risk, and the level of physical fitness.

Planning of physical training intensity corresponding to HR and the load obtained at AT is considered as a strategy appropriate to achieve expected results of motor rehabilitation.
Training intensity should be within the range from the lowest load necessary to achieve metabolic effects, and below values provoking adverse clinical symptoms or changes in the electrocardiogram (ischaemia, rhythm or conduction disorders). Training HR should be 10 bpm below the value at which signs of ischaemia occurred.[20] In ICD patients, during exercise HR should not exceed a value 20 bpm lower than the programmed device intervention threshold.

In practice, three training intensity ranges are used, and to determine them, the first ventilatory threshold (VT1) and the second ventilatory threshold (VT2) - the respiratory compensation point (RCP) identified during CPET, should be identified.

1. Light to moderate training: exercise of oxygen demand below VT1, during which stable lactate concentration is maintained at the rest values or slightly above (1-2 mmol/L)
2. Moderate to intense training) - called “aerobic-anaerobic transition”, limited by VT1 and RCP
3. Intense to maximum training - loads above RCP- to VO₂peak, without steady state achievement, with lactate concentration rising fast to 8 mmol/L, used, for example, in loading cycles of high intensity interval trainings (HIIT).[60]

**<4>CPET use to evaluate energy expenditure and nutrition status.**

The amount of energy spent during CPET is calculated using an energy equivalent of oxygen consumption, the value of which depends of RQ and is assessed in the base of the RER (see chapter Physiology of exercise). For the RER of 0.71, the energy equivalent is 4.68 kcal, while for RER of 1.0, the energy equivalent is 5.05. Therefore, measuring only the oxygen cost – VO₂ [L/min or ml/kg/min] and knowing the energy equivalent of oxygen consumption, a caloric cost of a given activity can be calculated.[180]

**<4>Evaluation of cardiac rehabilitation results**
The most important effects of physical training in selected groups of patients undergoing cardiac rehabilitation [181]:

1. improvement of exercise tolerance,
2. lower dyspnoea in heart failure,
3. improvement in epithelial function, including epithelium-dependent vasodilation,
4. reduction of blood concentration of angiotensin II, aldosterone, and natriuretic peptides
5. increase in diffusing lung capacity,
6. increase in “aerobic” regeneration ATP - lower lactate concentration at a given load,
7. improvement in metabolism and function of skeletal muscles,
8. lower rate of hospitalisation for exacerbated heart failure,
9. decrease in all cause mortality.

Effects of physical training evaluated in CPET:

1. increase in VO$_2$peak and C(a- v) O$_2$,
2. decrease in VO$_2$ when AT is exceeded,
3. increase in VO$_2$-AT - optimisation of oxygen consumption in working muscles,
4. increase in OUES,
5. lower VE vs VCO$_2$ slope,
6. drop in VE in relation to VCO$_2$ (“less linear” increase), most clearly visible post AT,
7. increase in HR reserve.

<4>CPET in cardiac rehabilitation - conclusions

- Indications: evaluation of physical exercise tolerance, determination of physical training intensity, evaluation of rehabilitation results, occupational rehabilitation, eprognostic evaluation,
- Main parameters: VO2max or VO2peak, VO$_2$-AT, VCO$_2$, HR and WR at VT1, VT2.
Athletes and healthy people

In the group of athletes and apparently healthy people the primary reason for CPET is a quantitative evaluation of aerobic physical capacity.\[5,26\] The cardiovascular system is primarily responsible for exercise capacity in that group. Respiratory, musculoskeletal and other systems play a secondary role. Aerobic capacity is higher in endurance (e.g. long-distance running, cycling, rowing, cross-country skiing), than in strength athletes (e.g. weightlifting). However, during the interpretation of exercise test results it should be taken into consideration that in the training process of any sports discipline various types of exercise: dynamic, static, and resistance, are used simultaneously but in different proportions.

Aerobic physical capacity is well characterised by VO$_2$\text{max}. VO$_2$\text{max} can be measured in the laboratory (e systems working with cycle ergometers and treadmills) or in natural conditions (similar to the environment in which the examined person trains - portable systems).

Categories of aerobic capability characterised by VO$_2$\text{max} as ml/kg/min for adult healthy people, depending on their sex and age, and according to various authors, are provided in Table S2 and Table S3.

Physical capacity in athletes - competitors and amateurs - is at least in very good or good category. The highest VO$_2$\text{max} in athletes are ca. 7 L/min (absolute value) and 94 ml/kg/min (relative value).[2] However, usually these values are within the range of 40–85 ml/kg/min depending on the discipline trained.[182]

Athlete’s physical capacity, regardless of the discipline trained, is a background on which technical skills are built. Aerobic physical capacity is used for qualification to a specific sports discipline. The “very good” category may be a precondition for achieving good sports results and good tolerance of endurance training in disciplines, in which dynamic exercise
prevails, while physical capacity in the “average” category may not be an obstacle to achieving very good results in other disciplines.

CPET results not only help to qualify people for the optimum type of training, but also help to monitor training results. For this purpose, VO$_2$-AT (VT1 and VT2) is also used, beside VO$_2$max. Both thresholds are useful in the planning of physical training intensity. VT1 determines the intensity of exercise that can be performed for a long time, while VT2 represents a lower limit at which the ability to perform anaerobic exercise improves.

In physically untrained people, AT occurs at loads corresponding to 40 to 65% VO$_2$max, while in well-trained athletes of endurance disciplines it shifts to 80–90% VO$_2$max. The higher the anaerobic threshold, the higher the ability for this type of exercise. In well-trained athletes, the anaerobic threshold is shifted to higher values (with no changes in VO$_2$max), and this may indicate correctly and effectively conducted training.

Every CPET conducted in an athlete or a apparently healthy person consists of the initial determination of predicted values, maximum or peak parameters, and values characterising AT.

In a group of adults who either train or plan to train recreationally, as well as in people of low and average physical activity, VO$_2$max value not only characterises their ability for physical exercise, but also their health status and the risk of cardiovascular diseases. The lower the physical capacity, the lower the cardiovascular capacity and the higher the risk of chronic non-infectious diseases. People with maximum physical capacity above 7.9 METs are characterised by lower all-cause and cardiovascular mortality, when compared to other people.[183] Higher physical capacity in a group of apparently healthy men is associated with a reduction in cardiovascular and all-cause mortality regardless of other risk factors.[184]
Concluding, it should be stated that the use of CPET results in the group of athletes and clinically healthy people is very extensive, as shown in Table 12.

**4> CPET in the evaluation of athletes and healthy people - conclusions**

- Indications: qualification for optimal training, monitoring of training results.
- Main parameters: VO$_{2}$peak, VO$_{2}$max, VO$_{2}$-AT (VT1 and VT2).

**3> New applications**

CPET combined with imaging techniques is a relatively new and promising concept. In imaging CPET (CPET-SE), CPET and exercise stress echocardiography (SE) are performed simultaneously. The simultaneous use of these two techniques allows to correlate functional changes evaluated in diagnostic imaging with exercise dynamics of electrocardiographic and CPET parameters.[185-187] This test can be performed in patients with limited exercise tolerance, including heart failure patients, both HFrEF and HFpEF. It allows to determine the cause of exercise intolerance.[188] The evaluation of dynamics and the presence of flattening of the ∆VO$_{2}$/∆WR curve helps to identify patients with poor exercise tolerance, with an exercise-induced increase of pressure in the right ventricle, and patients with exercise-induced deteriorated function of the right ventricle.[186]

Until now, no standardised exercise test protocol was established for echocardiography during CPET. However, it seems that the semi-supine bicycle ergometer is the best option. When the test is performed in the semi-supine position, echocardiographic parameters can be determined during exercise. Visualisation depends on the acoustic window, respiratory movements of the chest and body movements. The ramp protocol is recommended, with an increase in the load fitted to the patient’s capacity (e.g. 25 wat/2 min or 12.5 wat/2 min). Image acquisition every 2 minutes or at rest, with a low load, at peak exercise and at recovery is recommended.
CPET-SE may be useful in diagnosis and evaluation of advancement of heart failure, valvular diseases, HCM, and PH.

**Heart failure with reduced ejection fraction (HFrEF)**

The test allows simultaneous evaluation of physical capacity, SV, left ventricular contractility and diastolic function, and right ventricular function exercise-induced mitral insufficiency, and exercise-induced pulmonary hypertension.[189-191], CPET has also a prognostic value. In HFrEF patients, the worst prognosis was found in patients with the lowest tricuspid annular plane systolic excursion to pulmonary artery systolic pressure ratio (TAPSE/PASP) and presence of EOV.[192]

**Heart failure with preserved ejection fraction (HFpEF)**

Heart failure with preserved ejection fraction still remains a diagnostic and therapeutic challenge. An advantage of CPET-SE is the possibility to simultaneously evaluate changes in the left ventricular filling pressure evaluated using an early mitral flow-velocity to diastolic mitral annular velocity (E/e’), and exercise-induced pressure in the right ventricle, with capacity parameters (VO\textsubscript{2peak}, VO\textsubscript{2}-AT, VE vs VCO\textsubscript{2} slope).[193] CPET enables early diagnosis and exclusion of other causes of exertional dyspnoea.[194] It allows characterising HFpEF patients depending on pulmonary pressure and the right ventricular function.[195] This test enables the determination of exercise intolerance mechanisms in patients with heart failure and borderline ejection fraction, and to distinguish between cardiovascular diseases and deconditioning.[196,197]

**Valvular diseases**

The determination of valvular disease progress is a recognised indication for SE. This test is recommended when there is a discrepancy between symptoms and valvular disease severity - the symptoms are present while the valvular disease is not severe or symptoms are not present or are ambiguous when severe valvular dysfunction is diagnosed or when valvular disease coexists with left ventricular systolic dysfunction.[198,199] The primary goal of the stress test is to evaluate the valvular disease
severity, and its pathophysiological consequences (e.g. pulmonary pressure increase, a
transvalvular gradient increase, development or exacerbation of the left ventricular
dysfunction).

There are strong theoretical indications for the use of CPET-SE in valvular defects; however,
to this date the number of clinical studies confirming the usefulness of this method is
insufficient.

**Hypertrophic cardiomyopathy (HCM)**    HCM management is primarily focused on
the prevention of sudden cardiac death and development of heart failure. The latest ESC
guidelines concerning HCM management recommend functional evaluation using CPET in
classes IB or IIa B, depending on the presence or the lack of symptoms. Exercise SE is
recommended in symptomatic patients when bedside maneuvers fail to induce the LVOT
gradient ≥50 mmHg (class I B). On the other hand, in asymptomatic patients exercise SE
should be considered when a decision concerning modification of lifestyle or treatment is
necessary (class IIb C).[200] A gradient ≥50 mmHg, at rest or during provocation, is a cut-off
point for surgical or procedural treatment, when the symptoms cannot be controlled by
pharmacotherapy.[201,202] Although exercise-induced contractile disturbances may occur in
HCM patients, despite no changes in the coronary arteries] they can also be caused by
significant coronary arteries stenoses.[203,204]

Parameters evaluated in CPET (VO₂peak, VO₂ at AT, VE vs VCO₂ slope) have a prognostic
value in HCM.[205] Causes of exercise intolerance in HCM include pathologies occurring or
exacerbated during exercise: LVOTO, mitral insufficiency, left ventricular dysfunction, and
also chronotropic incompetence. HCM patients have a better prognosis when they achieve
higher % VO₂pred with a lower LVOT gradient.[68] CPET-SE may provide complimentary
information and allows the determination of the level and mechanism of exercise
intolerance.[206,207]
**Pulmonary hypertension**  
Current ESC guidelines do not recommend a diagnosis of exercise-induced pulmonary hypertension due to an insufficient data; however, evaluation of exercise-induced changes in the right ventricular systolic pressure has a prognostic role in patients diagnosed with primary pulmonary hypertension.[89] Pulmonary pressure may also rise in many left-sided heart diseases, including valvular diseases and heart failure, and this may also be helpful in the evaluation of the disease progress. Both CPET and SE may be useful in diagnosing exercise-induced pulmonary hypertension in patients with increased risk, e.g. with systemic connective tissue disorders, particularly scleroderma.[208] Combined right ventricular dysfunction evaluated by systolic area change, with low O2pulse identifies high risk patients in idiopathic PAH.[209]

**CPET-SE - conclusions**

- Indications for the test: evaluation, and disease progression assessment in heart failure, valvular heart diseases, HCM, PH.
- Main parameters: CPET (VO$_2$peak, VO$_2$ at AT, VE vs VCO$_2$ slope, arrhythmias, chronotropic competence, SBP), SE (global and regional contractility, valvular flow, LVOT gradient).

**Archiving of results**  
Test results are issued to a patient as a hardcopy authorised by doctors monitoring and interpreting the test. The result report should include a title page with patient details and the test result interpretation, pages containing a graphic and numeric representation of CPET results, and averaged 12-leads electrocardiogram from each test stage with marked changes in ST.

For results in a digital form, it is recommended to store them in at least two copies (in case data is lost) - in the memory of a computer used for exercise tests and a backup copy (external memory, server).
Test duration, financing

CPET is a separate procedure and should be separately financed, taking into account work performed by a nurse/operator/physical therapist and a doctor supervising and interpreting test results.

The time required to prepare the patient, perform the test and interpret the results is at least 45 to 60 minutes.

Conclusions  
Cardiopulmonary exercise testing is one of the essential tests of contemporary clinical practice. Its extensive diagnostic possibilities cover not only patients with cardiovascular, but also those with respiratory and musculoskeletal diseases. CPET scope of application was recently expanded to patients with oncological diseases. This test not only helps to diagnose causes of exercise intolerance, but it also supports evaluation of the treatment, including planning and evaluation of cardiac rehabilitation. New opportunities are offered by combining CPET with imaging such as exercise stress echocardiography. These tests are complimentary and synergistic in their diagnostic and prognostic strength. The usefulness of the combination of these two methods has been demonstrated in recent studies, but still requires confirmation in daily clinical practice.


Astrand PO. Experimental studies of physical work capacity in relation to sex and age. Copenhagen: Munkgaard; 1952.


**Table 1** Method for predicted oxygen uptake calculation in men, as ml/min according to Wasserman/Hansen [35]

<table>
<thead>
<tr>
<th>Step 1: Calculate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle factor = 50.72 – 0.372 × Age [years]</td>
</tr>
<tr>
<td>Ideal weight (kg) = 0.79 × Height [cm] – 60.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 2: Classify body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual weight ≤/≥ ideal weight</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 3: Select an equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual weight &lt; ideal weight</td>
</tr>
<tr>
<td>( VO_2 = \frac{(\text{ideal weight} + \text{actual weight})}{2} \times \text{cycle factor} )</td>
</tr>
<tr>
<td>Actual weight = ideal weight</td>
</tr>
<tr>
<td>( VO_2 = \text{actual weight} \times \text{cycle factor} )</td>
</tr>
<tr>
<td>Actual weight &gt; ideal weight</td>
</tr>
<tr>
<td>( VO_2 = (\text{ideal weight} \times \text{cycle factor}) + 6 \times (\text{actual weight} - \text{ideal weight}) )</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 4: Include the load type</th>
</tr>
</thead>
<tbody>
<tr>
<td>For cycle</td>
</tr>
<tr>
<td>( VO_2 ) calculated in Step 3. is equal to ( VO_2 )pred depending on the body weight</td>
</tr>
<tr>
<td>For treadmill</td>
</tr>
<tr>
<td>( VO_2 )pred is equal to ( VO_2 ) from step 3 x 1.11</td>
</tr>
</tbody>
</table>
**Example:** a 55-year-old man, weight 78 kg, height 170 cm, achieved the VO2peak 2.600 ml/min during the CPET on treadmill.

Ideal weight 74 kg; cycle factor 30.26; VO2pred 2501.4 ml/min (this is the minimum predicted value, below which impairment of aerobic exercise capacity can be recognized).

Relative capacity % VO2pred = 100 × 2600 / 2501.4 = 103.9%.

Calculations results: good exercise capacity % VO2pred ≥100%.

Abbreviations: VO2pred – predicted oxygen uptake, VO2 – oxygen uptake at peak exercise

---

**Table 2** Method for predicted oxygen uptake calculation in women, as ml/min according to Wasserman/Hansen [35]

<table>
<thead>
<tr>
<th>Step 1: Calculate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle factor = 22.78 – 0.17 × Age [years]</td>
</tr>
<tr>
<td>Ideal weight (kg) = 0.65 × height [cm] - 42.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 2: Classify body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual weight &lt;=/&gt; ideal weight</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 3: Select an equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual weight &lt; ideal weight</td>
</tr>
<tr>
<td>VO2 = ([ideal weight + actual weight + 86]/2) × <em>cycle factor</em></td>
</tr>
<tr>
<td>Actual weight = ideal weight</td>
</tr>
<tr>
<td>VO2 = (actual weight + 43) × <em>cycle factor</em></td>
</tr>
<tr>
<td>Actual weight &gt; ideal weight</td>
</tr>
<tr>
<td>VO2 = (ideal weight + 43) × <em>cycle factor</em> + 6 × (actual weight - ideal weight)</td>
</tr>
</tbody>
</table>

| Step 4: Include the load type |
For cycle

\[ \text{VO}_2 \text{ calculated in Step 3. is equal to VO}_2\text{pred depending on the body weight} \]

For treadmill

\[ \text{VO}_2\text{pred is equal to VO}_2 \text{ from step 3 x 1.11} \]

Abbreviations: VO\text{\textsubscript{2}}\text{pred} – predicted oxygen uptake, VO\text sub{2} – oxygen uptake at peak exercise

---

**Table 3** Normal values and normal responses to exercise for key cardiopulmonary exercise testing variables [5,31]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal values/responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO\textsubscript{2}\text{peak}, ml/kg/min</td>
<td>Wide range depending on age, sex, physical activity– 15–80 ml/kg mc./min</td>
</tr>
<tr>
<td>% VO\textsubscript{2}\text{pred}, %</td>
<td>≥100%</td>
</tr>
<tr>
<td>VO\textsubscript{2} – AT, ml/kg mc./min</td>
<td>≥40–50% VO\textsubscript{2}\text{pred (age dependent)}</td>
</tr>
<tr>
<td>RER at peak exercise</td>
<td>≥1.10 (indicates excellent exercise effort)</td>
</tr>
<tr>
<td>VE vs VCO\textsubscript{2} slope</td>
<td>&lt;30 considered as normal, slide increase with age</td>
</tr>
<tr>
<td>PETCO\textsubscript{2}, mm Hg</td>
<td>at rest 36–42 mmHg</td>
</tr>
<tr>
<td></td>
<td>increase 3–8 mm Hg during exercise up to AT</td>
</tr>
<tr>
<td></td>
<td>decrease following AT according to increased ventilation</td>
</tr>
<tr>
<td>VE/VO\textsubscript{2} at peak exercise</td>
<td>≤40</td>
</tr>
<tr>
<td></td>
<td>50 – upper limit of normal response</td>
</tr>
<tr>
<td>BR at peak exercise</td>
<td>&gt;15%</td>
</tr>
<tr>
<td>VE at peak exercise/MVV</td>
<td>≤ 0.8</td>
</tr>
<tr>
<td>(\Delta\text{VO}_2/\Delta\text{WR}, \text{ml/min/wat})</td>
<td>increase 8,4–11,0 ml/min/wat</td>
</tr>
<tr>
<td>HR during exercise bpm</td>
<td>increase 10 bpm per 3,5 ml/kg mc./min increase VO₂</td>
</tr>
<tr>
<td>------------------------</td>
<td>---------------------------------------------------</td>
</tr>
<tr>
<td>HR recovery at 1 min standing, bpm</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>SBP increase 10 mm Hg per 3,5 ml/kg mc./min increase VO₂ up to 210 mm Hg (men) i 190 mm Hg (women) DBP – unchanged or slight decrease</td>
</tr>
<tr>
<td>SpO₂, %</td>
<td>≥95% at rest and during exercise Should not decrease &gt;5% (absolute value)</td>
</tr>
</tbody>
</table>

Abbrevations: % VO₂pred – percent predicted oxygen uptake; BR – breath reserve; DBP – diastolic blood pressure; HR – heart rate; MVV – maximal voluntary ventilation; PETCO₂ – end-tidal carbon dioxide partial pressure; RER – respiratory exchange ratio; SBP – systolic blood pressure; SpO₂ – oxygen saturation by pulse oximetry; VE – minute ventilation; VE vs VCO₂ slope – ventilatory efficiency; VO₂ – oxygen uptake; VO₂-AT – oxygen uptake at anaerobic threshold; VO₂peak – oxygen uptake at peak exercise

<table>
<thead>
<tr>
<th>Tabela 4 Questions useful in cardiopulmonary exercise testing assessment according to Wasserman et al. [31]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Question</strong></td>
</tr>
<tr>
<td>Is exercise capacity reduced?</td>
</tr>
<tr>
<td>Question</td>
</tr>
<tr>
<td>------------------------------------------------------</td>
</tr>
<tr>
<td>Is the metabolic requirement increased?</td>
</tr>
<tr>
<td>Is oxygen uptake impaired?</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Is ventilatory capacity reduced?</td>
</tr>
<tr>
<td>Is there ventilation-perfusion mismatch?</td>
</tr>
<tr>
<td>Are there defects of muscle oxygen utilization?</td>
</tr>
<tr>
<td>Are there any behavioral problems?</td>
</tr>
</tbody>
</table>
Is there effort sufficient enough?

Poor effort

Increased HR reserve; increased BR; RER at peak exercise <1.0; normal AT P(A-a)O\(_2\); P(a-ET)CO\(_2\) (panels 1, 2, 3, 8, 9)

Abbrevations: AT, anaerobic threshold; BR, breathing reserve; HR, heart rate; P(A - a)O\(_2\) alveolar to arterial PO\(_2\) difference; P(a-ET)CO\(_2\) arterial to end-tidal PCO\(_2\) difference, RER, respiratory exchange ratio; VCO\(_2\), carbon dioxide output; VD, dead space volume; VE, minute ventilation; VO\(_2\), oxygen uptake; VO\(_2\)peak, oxygen uptake at peak exercise; VT, tidal volume; WR, work rate.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cardiac disease</th>
<th>Pulmonary disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO(_2)peak</td>
<td>reduced</td>
<td>reduced</td>
</tr>
<tr>
<td>VO(_2)-AT</td>
<td>reduced</td>
<td>normal or reduced</td>
</tr>
<tr>
<td>Δ VO(_2)/Δ WR</td>
<td>often reduced</td>
<td>normal</td>
</tr>
<tr>
<td>HR at peak exercise</td>
<td>can be reduced</td>
<td>can be reduced</td>
</tr>
<tr>
<td>O(_2)pulse at peak exercise</td>
<td>often reduced</td>
<td>can be reduced</td>
</tr>
<tr>
<td>BR</td>
<td>&gt;20%</td>
<td>&lt;15%</td>
</tr>
<tr>
<td>FEV(_1) at recovery</td>
<td>as before exercise</td>
<td>can be reduced</td>
</tr>
<tr>
<td>PaO(_2) or SaO(_2)</td>
<td>normal</td>
<td>often reduced</td>
</tr>
<tr>
<td>VD/VT</td>
<td>can be increased</td>
<td>often increased</td>
</tr>
</tbody>
</table>
VE vs VCO₂ slope often increased can be increased

Abbreviations: BR – breath reserve; FEV₁ – forced expiratory volume at one second; HR – heart rate; O₂ pulse – oxygen pulse; PaO₂ – arterial pressure of oxygen in an arterial blood; SaO₂ – arterial oxygen saturation by gasometry; VE vs VCO₂ slope – ventilatory efficiency; VD – dead space volume; VO₂-AT – oxygen uptake at anaerobic threshold; VO₂peak – oxygen uptake at peak exercise; VT – tidal volume

| Table 6 Weber’s exercise functional classification |
|---|---|---|
| **Class** | **Severity of functional impairment** | **VO₂peak, ml/kg mc./min** |
| A | little or no impairment | >20 |
| B | mild to moderate | 16–20 |
| C | moderate to severe | 10–15,9 |
| D | severe | <10 |

Abbreviations: VO₂peak, oxygen uptake at peak exercise

| Table 7 Ventilatory classes |
|---|---|
| **Class** | **VE vs VCO₂ slope** |
| I | <30,0 |
| II | 30,0–35,9 |
| III | 36,0–44,9 |
| IV | ≥45,0 |

Abbreviations: VE vs VCO₂ slope – ventilatory efficiency
<table>
<thead>
<tr>
<th>ACHD</th>
<th>VO_{2\text{peak}}</th>
<th>VE vs VCO_{2} slope</th>
<th>VO_{2}-AT</th>
<th>HR max</th>
<th>O_{2} pulse</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>rToF</td>
<td>↓↓↓</td>
<td>↑↑↑</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↓↓↓</td>
<td>most common in patients with pulmonary regurgitation</td>
</tr>
<tr>
<td>Ebstein’s anomaly</td>
<td>↓↓↓</td>
<td>↑↑</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↓↓↓</td>
<td></td>
</tr>
<tr>
<td>TGA after M/S procedure</td>
<td>↓↓↓</td>
<td>↑↑</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↓↓↓</td>
<td>see comment on the bottom</td>
</tr>
<tr>
<td>CoA</td>
<td>↓↓</td>
<td>↑</td>
<td>↓↓↓</td>
<td>↓</td>
<td>↓↓</td>
<td>hypertensive SBP response to exercise has prognostic value</td>
</tr>
</tbody>
</table>
Patients after TCPC have better exercise capacity than after APC

Drop in SaO2
Often do not achieve VT

Skróty: APC – połączenie przedsionkowo-płucne; CoA – koarktacja aorty; HR – częstotliwość rytmu serca;
TGAO₂pulse – puls tlenowy; rToF – całkowita korekcja tetralogii Fallota (przed ew. interwencją na zastawce płucnej); SaO₂ – saturacja hemoglobiny tlenem krwi tetniczej – pomiar metodą gazometrii; TGA after M/S – transposition of great arteries after Mustard/Sennning repair; TCPC – total cavopulmonary connection; VO₂-AT – oxygen uptake at anaerobic threshold; VE vs VCO₂ slope – ventilatory efficiency; VO₂peak – oxygen uptake at peak exercise; VT – tidal volume
Arrows: ↑, occasionally elevated; ↑↑, sometimes elevated; ↑↑↑, often elevated; ↑↑↑↑, most often elevated; ↓, occasionally decreased; ↓↓ – sometimes decreased; ↓↓↓, often decreased; ↓↓↓↓, most often decreased

Ad: patients with TGA after anatomical correction (arterial switch; Jatene procedure) are usually asymptomatic; signs of ischaemia can be present during CPET
### Table 9: Changes in ventilation parameters in pulmonary arterial hypertension

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>PETCO₂ at rest</td>
<td>reduced</td>
</tr>
<tr>
<td>PETCO₂ w AT</td>
<td>markedly reduced</td>
</tr>
<tr>
<td>VD/VT during exercise</td>
<td>increased</td>
</tr>
<tr>
<td>VE vs VCO₂ slope during exercise</td>
<td>markedly increased</td>
</tr>
<tr>
<td>SpO₂ during exercise</td>
<td>reduced</td>
</tr>
</tbody>
</table>

Abbreviations: AT – anaerobic threshold; PETCO₂ – end-tidal carbon dioxide partial pressure; VD – dead space volume; VE vs VCO₂ slope – ventilatory efficiency; VT – tidal volume; SpO₂ – oxygen saturation by pulse oximetry

### Table 10: Use of cardiopulmonary exercise testing parameters for the evaluation of one year mortality risk in pulmonary arterial hypertension

<table>
<thead>
<tr>
<th>Risk</th>
<th>VO₂peak</th>
<th>VE vs VCO₂ slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (&lt;5%)</td>
<td>&gt;15 ml/kg mc./min</td>
<td>&lt;36</td>
</tr>
<tr>
<td>Moderate (5–10%)</td>
<td>11–15 ml/kg mc./min</td>
<td>36–44,9</td>
</tr>
<tr>
<td>High (&gt;10%)</td>
<td>&lt;11 ml/kg mc./min</td>
<td>≥45</td>
</tr>
</tbody>
</table>

Abbreviations: VE vs VCO₂ slope – ventilatory efficiency; VO₂peak – oxygen uptake at peak exercise

### Table 11: Diagnostic stratification for patients with suspected myocardial ischaemia according to Guazzi M and Arena R et al. (modified)

<table>
<thead>
<tr>
<th>Data from CPET</th>
<th>Risk of ischaemic heart disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>Low</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>O₂pulse vs WR trajectory</th>
<th>VO₂ vs WR trajectory</th>
<th>% VO₂&lt;sub&gt;pred&lt;/sub&gt;</th>
<th>HR vs WR trajectory</th>
</tr>
</thead>
<tbody>
<tr>
<td>trajectory</td>
<td>Continual rise</td>
<td>Early and sustained</td>
<td>≥100%</td>
<td>Linearity rise HR vs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>plateau</td>
<td>99–75%</td>
<td>WR with possible</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>74–50%</td>
<td>flatening only at</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>peak exercise</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;50%</td>
<td>Higher HR increase</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>after AT</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Rise</td>
<td>Flat response</td>
<td>Drop</td>
<td></td>
</tr>
<tr>
<td>ECG</td>
<td>Absence of arrhythmia,</td>
<td>Arrhythmia, conduction</td>
<td>Arrhythmia,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>conduction disturbances,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ST changes</td>
<td>changes not lead to</td>
<td>conduction</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>test termination</td>
<td>disturbances, ST</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>changes lead to test</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>termination</td>
<td></td>
</tr>
<tr>
<td>Patient reason</td>
<td>Muscle fatigue</td>
<td>Angina</td>
<td>Dyspnea</td>
<td></td>
</tr>
<tr>
<td>for test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>termination</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AT – próg beztlenowy; CPET – cardiopulmonary exercise testing; ECG – electrocardiogram; HR – heart rate; O₂pulse – oxygen pulse; VO₂ – oxygen uptake; % VO₂<sub>pred</sub> – percent predicted oxygen uptake; WR – work rate

Table 12  Indications for cardiopulmonary exercise testing in athletes and apparently healthy people
<table>
<thead>
<tr>
<th><strong>Aim</strong></th>
<th><strong>Athletes</strong></th>
<th><strong>Apparently healthy people</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantitative assessment of exercise capacity: $\text{VO}_2\text{max}$</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Assessment and application of training strategies: $\text{VO}_2\text{-AT}$</td>
<td>+</td>
<td>+ (optionally)</td>
</tr>
<tr>
<td>Monitorowanie efektów skuteczności treningu fizycznego: $\text{VO}_2\text{-AT}$</td>
<td>+</td>
<td>+ (optionally)</td>
</tr>
<tr>
<td>Health status assessment:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– cardiovascular system: HR, blood pressure, ECG</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>– respiratory system: spirometry and ventilatory parameters</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>– exercise metabolism assessment</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Qualification for a chosen sport discipline</td>
<td>+</td>
<td>+ (optionally)</td>
</tr>
<tr>
<td>Cardiovascular risk factors evaluation: „low exercise capacity”</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

Abbreviations: ECG – electrocardiogram; HR – heart rate; $\text{VO}_2\text{max}$ – maximal oxygen uptake; averaged value from 10–60 s according to protocol used; $\text{VO}_2\text{-AT}$ – oxygen uptake at anaerobic threshold
Figure 1

Algorithm for the differential diagnosis of the cause of exercise limitation (according to Wasserman, modified).

AT – anaerobic threshold; BF – breathing frequency; BR – breathing reserve; Hgb – haemoglobin concentration; HR – heart rate; SpO₂ oxygen saturation by pulse oximetry; VD – dead space volume; VE – minute ventilation; VCO₂ – carbon dioxide output; VO₂ - AT – oxygen uptake at anaerobic threshold; VO₂peak – oxygen uptake at peak exercise; VT, tidal volume.
Figure 2

The algorithm based on cardiopulmonary exercise tests results, for risk stratification in patients with heart failure with reduced ejection fraction according to The Committee on Exercise Physiology and Training of the Heart Failure Association of the European Society of Cardiology [43]

HFrEF – heart failure with reduced ejection fraction, RER – respiratory exchange ratio, VE vs VCO2 slope – ventilatory efficiency, VO2peak – oxygen uptake at peak exercise.
Figure 3

Normal and pathological courses of oxygen pulse vs work rate. O$_2$ pulse – oxygen pulse; WR – work rate

Figure 4

Trends of heart rate (y 1 - axis) and oxygen (y 2- axis) in relation to work rate (x-axis) in patient with exertional myocardial ischaemia. HR – heart rate; O$_2$ pulse – oxygen pulse; WR – work rate
Figure 5

Normal and pathological courses of oxygen uptake (VO₂) (y 1-axis) in relation to work rate (WR) – solid line (y 2-axis). VO₂ – oxygen uptake; WR – work rate

Figure 6

Flow – volume loop