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The CPET-HFpEF Score: a noninvasive test for the diagnosis of heart failure with preserved ejection fraction

T. Nitschke[1], C. Baukmann[1], H. Heuer[2]

Abstract: *Introduction:* The diagnosis of heart failure with preserved ejection fraction (HFpEF) is still challenging, with the gold standard being invasive testing. For noninvasive diagnosis two multiparameter risk scores exist, the HFA-PEFF and the H2FPEF-scoring systems. Both integrate morphological evidence of structural heart disease from echocardiography, historical features or laboratory assessment of natriuretic peptides. However, there is still a gap in accuracy when these results are inconclusive. Here, we present a noninvasive test for the diagnosis of HFpEF that is based on cardiopulmonary exercise testing (CPET) parameters.

Methods / results: CPET is the gold standard for identifying the cause of unexplained dyspnoea and/or exercise intolerance, the main symptoms of heart failure. CPET was performed with a total of 100 patients, 50 with HFpEF estimated by the HFA-PEFF score of 6 and 50 patients without a diagnosis of heart failure. For our score we only used parameters with the highest diagnostic accuracy for diagnosing heart failure, which was estimated via an unpaired t-test. Thresholds for the diagnosis of HFpEF were estimated via logistic regression analysis and adjusted by the known threshold, described in the literature. The accuracy of various combinations of parameters for the score was tested via ROC-curve-analysis. By combining five parameters of the CPET (VO_2peak indexed by body weight, VE/VCO_2 slope, oxygen uptake efficiency slope [OUES], VO_2/WR slope and the increase in $PetCO_2$ during exercise [$PetCO_2$ delta]) we obtained a sensitivity of 91% and a specificity of 96% for the diagnosis of HFpEF. By adding the NT-proBNP value, the sensitivity improved to 100% and the specificity remained at 96%.

Conclusion: The CPET-HFpEF score allows the confirmation of the diagnosis of HFpEF in patients with exercise intolerance and dyspnoea with one comprehensive whole-body testing technique. In combination with the determination of NT-proBNP, the high diagnostic accuracy can be further improved.

Keywords: heart failure, HFpEF, cardiopulmonary exercise testing, CPET

Kurzfassung: Der CPET-HFpEF-Score: ein nichtinvasiver Test zur Diagnose der Herzinsuffizienz mit erhaltener Ejektionsfraktion. *Einleitung:* Die Diagnose der Herzinsuffizienz mit erhaltener Ejektionsfraktion (HFpEF) ist nach wie vor schwierig, der Goldstandard ist eine invasive Rechtsherzkatheteruntersuchung. Für die nichtinvasive Diagnose gibt es zwei Multiparameter-Risikoscores, das HFA-PEFF- und das H2FPEF-Scoring-System. Beide integrieren morphologische Anzeichen einer strukturellen Herzerkrankung aus der Echokardiographie, Daten der Krankengeschichte und der HFA-PEFF-Score die Bestimmung von natriuretischen Peptiden. Es gibt jedoch immer noch eine Lücke in der Genauigkeit, wenn der Score nicht eindeutig ist. Wir haben einen nicht-invasiven Test zur Diagnose von HFpEF entwickelt, der Parameter der Spiroergometrie (CPET) verwendet.

Methoden / Ergebnisse: Die Spiroergometrie ist der Goldstandard für die Identifizierung der Ursache von ungeklärter Dyspnoe und/oder Belastungsintoleranz, den Hauptsymptomen der Herzinsuffizienz. Wir führten den Test bei 100 Patienten durch, von denen bei 50 Personen HFpEF diagnostiziert wurde (ein Wert von 6 im HFA-PEFF-Score) und 50 Patienten ohne Diagnose einer Herzinsuffizienz waren. Für den Score wurden die Parameter der Spiroergometrie mit der höchsten diagnostischen Genauigkeit verwendet, die durch einen ungepaarten t-Test ausgewertet wurden. Die Schwellenwerte wurden mit Hilfe einer logistischen Regressionsanalyse abgeschätzt und an die in der Literatur beschriebenen Schwellenwerte angepasst. Die Genauigkeit der Ergebnisse wurden durch eine ROC-Kurven-Analyse geprüft. Durch die Kombination von fünf Spiroergometrie-Parametern (VO_2peak/Körpergewicht, VE/VCO_2-Slope, Sauerstoffaufnahmeeffizienz-Slope [OUES], Energieeffizienz [VO_2/WR-Slope] und der Anstieg von $PetCO_2$ während der Belastung [$PetCO_2$ delta]) erhielten wir eine Sensitivität von 91 % und eine Spezifität von 96 % für die Diagnose HFpEF. Durch Bewertung des NT-proBNP-Wertes verbesserte sich die Sensitivität auf 100 % bei einer gleichbleibenden Spezifität von 96 %.

Schlussfolgerung: Der CPET-HFpEF-Score ermöglicht es, die Diagnose HFpEF bei Patienten mit Belastungsintoleranz und Dyspnoe durch die Spioroergometrie zu bestätigen. In Kombination mit der Bestimmung von NT-proBNP kann die hohe diagnostische Genauigkeit weiter verbessert werden.
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Schlüsselwörter: Herzinsuffizienz, HFpEF, Spiroergometrie, CPET

Introduction

Heart failure with preserved ejection fraction (HFpEF) is often underdiagnosed. Nearly half of all patients with heart failure have a heart failure with preserved ejection fraction. HFpEF is a syndrome characterized by symptoms and signs of heart failure, an ejection fraction ≥ 50 and no previous LVEF < 50%, evidence of elevated filling pressure at rest or during exercise, and elevated levels of natriuretic peptides. The gold standard diagnostic test involves testing and exercising haemodynamic assessments during right heart catheterization, but this test is not universally available [1].

The clinical diagnosis is still challenging, and the key clinical correlates are exercise intolerance and dyspnoea [2]. The absence of noninvasive gold standard tests is of increasing concern [3]. Two scoring tools have been developed to assist in the noninvasive diagnosis of HFpEF in patients with exercise intolerance and exertional dyspnoea: The HFA-PEFF includes parameters from echocardiography, such as signs of functional and structural abnormalities and the measurement of natriuretic peptides [4]. The H2FPEF score incorporates parameters of the medical history and measurements of echocardiography [5]. However, there is still a diagnostic gap if the results are intermediate. The recommendations advise the performance of an exercise test.

Cardiopulmonary exercise testing (CPET) is the most comprehensive whole-body testing technique for assessing, quantifying and differentiating the reasons for exercise intolerance and dyspnoea [6]. According to the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure, there is a IIa recommendation for cardiopulmonary exercise testing to

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Abbreviations

AUC	area under the curve
BMI	body mass index
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
CO_2	carbon dioxide
CPET	cardiopulmonary exercise testing
ECG	electrocardiogram
E/E´	ratio of early diastolic mitral inflow to mitral annular tissue velocities
EF	ejection fraction
FEV	forced expiratory volume
FEV_1	forced expiratory volume in 1 second
GFR	glomerular filtration rate
HFpEF	heart failure with preserved ejection fraction
HR	heart rate
HRR	heart rate recovery
MMV	maximal voluntary ventilation
O_2	oxygen
OUES	oxygen uptake efficiency slope
PA	pulmonary artery
$PACO_2$	partial pressure of CO_2 in arterial blood
$PetCO_2$	end tidal pressure of carbon dioxide
$PetCO_2$ delta	difference in the increase in PetCO2
RER	respiratory exchange ratio
ROC	receiver operating characteristics
RR	respiratory rate
VE	ventilation
VE/VCO_2	carbon dioxide minute VE equivalent
VE/VCO_2 slope	slope of carbon dioxide minute VE equivalent
VE/VO_2	oxygen minute VE equivalent
VO_2	oxygen uptake
VO_2/HR	oxygen pulse
VO_2/WR ratio	aerobic capacity
VO_2peak	peak oxygen consumption
$VO_2/VT_1\%$	oxygen uptake at the first ventilatory treshold
VT	tidal volume
VT_1	first ventilatory threshold
VT_2	second ventilatory threshold

identify the cause of unexplained dyspnoea and/or exercise intolerance [7]. It is a safe technique and a suitable choice for the assessment of most patients. During CPET, ventilation, oxygen uptake and carbon dioxide output are measured breath-to-breath. The CPET also reports parameters incorporated in a standard exercise stress test. These include repeated registration of the ECG, stress and recovery heart rate, blood pressure, exercise workload and exercise time. While many parameters of the CPET are affected by heart failure, most lack specificity for the condition. The diagnosis of heart failure by CPET is therefore still challenging, but CPET is the standard for assessing, quantifying, and differentiating the origin of dyspnoea and exercise impairment [8].

The purpose of this work was to improve the quality of diagnosis for HFpEF patients by developing a score using CPET parameters, which are typically altered in heart failure patients. Because dyspnoea and exercise intolerance are typical clinical signs of HFpEF, an exercise test is the best way to detect heart failure. In 2018 VO_2peak measured noninvasively via CPET was examined by Borlaug and colleagues for the diagnosis of HFpEF. A VO_2peak < 14 ml/kg/min or > 20 mm/kg/min was useful to rule-in and rule-out HFpEF, but patients with a mildly depressed VO_2peak value require additional testing to clarify the diagnosis because noncardiac disease may also lead to a reduced VO_2peak [9].

Methods

This study included 100 participants. The inclusion criterion for 50 patients with HFpEF was a diagnosis of HFpEF corresponding to the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure, which was additional validated by the HFA-PEFF-algorithm with a maximal score of 6. This diagnostic algorithm showed acceptable specificity and sensitivity for the diagnosis and exclusion of HFpEF [10]. For all patients an evaluation of their medical history, CPET, NT-proBNP and echocardiography were performed. Patients with a reduced breathing reserve, decreased oxygen saturation during exercise or signs of pulmonary disease were excluded.

The control group included 50 participants with no evidence of heart failure or cardiac disease. The medical history was recorded, and a CPET and echocardiography were performed.

CPET

Every patient performed a symptom limited CPET on a cycle ergometer (Ergoselect, Ergoline, Software Custo Diagnostic, Version 4.5.8) via an incremental exercise protocol. The planned exercise duration was tailored to reach 8–12 min maximal duration. We used a multistage exercise protocol with increasing intensity every 2 minutes. The initial workload was personalized for each patient. Patients were instructed to exert maximal effort. If a respiratory exchange rate (RER) greater than 1.05 was reached, the CPET was considered complete. Pharmacological therapy was continued before and throughout exercise testing.

The ventilatory expired gas analysis was performed by using a metabolic card Metalyzer 3B-R2, Cortex, together with the software Meta Soft Studio version 5.8.7. Before each test, the equipment was calibrated in a standard fashion. First, spirometry was performed to estimate the FEV_1 and FEV values. ECG and blood pressure data were documented routinely during the test. Ventilation, oxygen uptake and carbon dioxide production data were acquired breath by breath. For data interpretation the measurements were averaged every 20 seconds.

The following parameters were analysed for the use of our score:

VO_2peak (VO_2 at peak exercise)

Peak oxygen consumption is the most important parameter for measuring exercise capacity. VO_2peak is also a significant prog-

nostic factor [11]. During a progressive exercise stimulus, the VO_2 value increases linearly in proportion to work. VO_2max has been defined by a plateau, but it is often not observed. Therefore, VO_2peak is the highest value of O_2-consumption and is commonly used as the expression of maximal oxygen uptake. VO_2peak can be reported as an absolute value, indexed per body weight (peak VO_2 ml/kg/kg) or as a percentage of the predicted value (VO_2peak %) [12].

In heart failure the reduction in VO_2peak is sensitive for HFpEF but nonspecific. The oxygen uptake at the first ventilatory threshold (VT_1) (VO_2/VT_1%) is normally 40–75% of the predicted oxygen uptake. The lack of VO_2 at VT_1 has a strong independent prognostic role [13]. For the determination of VO_2 at VT_1 we used a combination of several methods. With the V-slope method we determined the point at which the incremental volume of VCO_2 becomes greater than that of VO_2 because of the additional CO_2 produced by lactic acid buffering. Second, we used the end-tidal CO_2 versus the end-tidal O_2 method, the point when end-tidal O_2 increased, and end-tidal CO_2 slightly decreased. Third we applied the oxygen minute VE equivalent (VE/VO_2) versus the carbon dioxide minute VE equivalent (VE/VCO_2), and we used the point of continuous increase in VE/VCO_2.

VE/VCO_2 slope

The VE/VCO_2 slope reflects ventilatory efficiency and is a powerful prognostic marker. An elevated VE/VCO_2 slope during exercise is attributed to the combination of hyperventilation and increased dead space ventilation. The VE/VCO_2 slope is increased in patients with HFpEF, but it is also increased in a broad spectrum of other diseases [6, 14]. The VE/VCO_2 slope was estimated between one minute after starting exercise and VT_2.

VO_2/HR (O_2 pulse)

The oxygen pulse is the ratio of VO_2 to heart rate and reflects the amount of oxygen extracted per heartbeat. The O_2 pulse is correlated with cardiac output. A low O_2 pulse can be related not only to a reduced stroke volume, but also to decreased skeletal muscle O_2 extraction. The increase should be linear. A flattening of the curve or the occurrence of a plateau can be signs of myocardial dysfunction. The O_2 pulse is affected by the intake of betablockers [14, 15].

VO_2/WR ratio (aerobic capacity)

The VO_2/WR ratio describes the change in oxygen-uptake in correlation with stress and reflects the ability of oxygen to be delivered to working muscles. It increases linearly during exercise, as a progressive workload demands progressive oxygen consumption. In heart failure reduced values imply impaired O_2 delivery [6, 16]. The VO_2/WR ratio was estimated beginning one minute after starting the exercise and ending at the second ventilatory threshold (VT2).

OUES

The oxygen uptake efficiency slope (OUES) describes the relationship between oxygen uptake and ventilation during incremental exercise. A logarithmic transformation of the increase in ventilation results in linear behaviour with a slope that is not dependent on the maximal exercise. OUES is defined as the regression slope "a" in $VO_2 = a \log VE + b$. The OUES was estimated in the same time frame as the VO_2/WR ratio. Patients with heart failure have significantly lower OUES values than patients without heart failure [17, 18].

Heart rate recovery

Heart rate recovery (HRR) is defined as a reduction in heart rate from peak exercise to one minute later. In heart failure a decreased HHR can be detected and predicts mortality [19].

$PetCO_2$ kinetics

$PetCO_2$ is the end-tidal concentration of CO_2 in the exhaled air and correlates with $PaCO_2$. At rest $PaCO_2$ is approximately 2 mmHg higher than PetCO2, and during exercise $PetCO_2$ is approximately 4 mmHg higher than $PaCO_2$ [20]. Typically, the $PetCO_2$ is approximately 33 mmHg at baseline and increases 3–6 mmHg during exercise. In patients with heart failure the production of CO_2 is reduced, and the increase is less than 3–5 mmHg. The difference in the increase in $PetCO_2$ (difference between $PetCO_2$ at the beginning of the examination versus the highest value of $PetCO_2$ during examination) will be called „$PetCO_2$ delta" in the following text. In chronic obstructive pulmonary disease (COPD) the increase is also reduced, but $PetCO_2$ in HF decreases at peak exercise, whereas it plateaus in COPD [21].

Respiratory exchange rate (RER)

The RER is calculated as the ratio between the carbon-dioxide output and oxygen uptake. The RER increases with exercise, and a RER value exceeding 1.05 indicates a good effort.

Breathing reserve

Breathing reserve is the percentage of a subjects' maximal voluntary ventilation (MVV) that is not used at peak exercise. The MVV is approximated by multiplying the forced expiratory volume (FEV) by 35. Values less than 20% suggest a ventilatory limitation and may help to discriminate between patients with heart failure and those with a pulmonary disease [22].

Statistical analysis

Statistical calculations were performed using R studio Version 2024.04.0+735. The selected parameters were tested by an unpaired t-test. For the score we choose the significant parameters explained previously and performed a receiver operating characteristic curve (ROC curve) analysis. After this, we determined the parameters for the score and performed a logistic regression analysis of each parameter. The location parameter was also used for estimating the best threshold. With different parameters and thresholds, we performed ROC-curve analysis to identify the most significant score-system.

This investigation conforms with the principles outlined in the Declaration of Helsinki. This study was approved by the ethics committee of the University Witten-Herdecke. Written informed consent was obtained from all participants.

Results

The mean age of the population was 74.4 ± 12.0 years, and 32% of the participants were women. The mean body mass index was 27.2 kg/m². Subjects with HFpEF were older and had more comorbidities (Table 1).

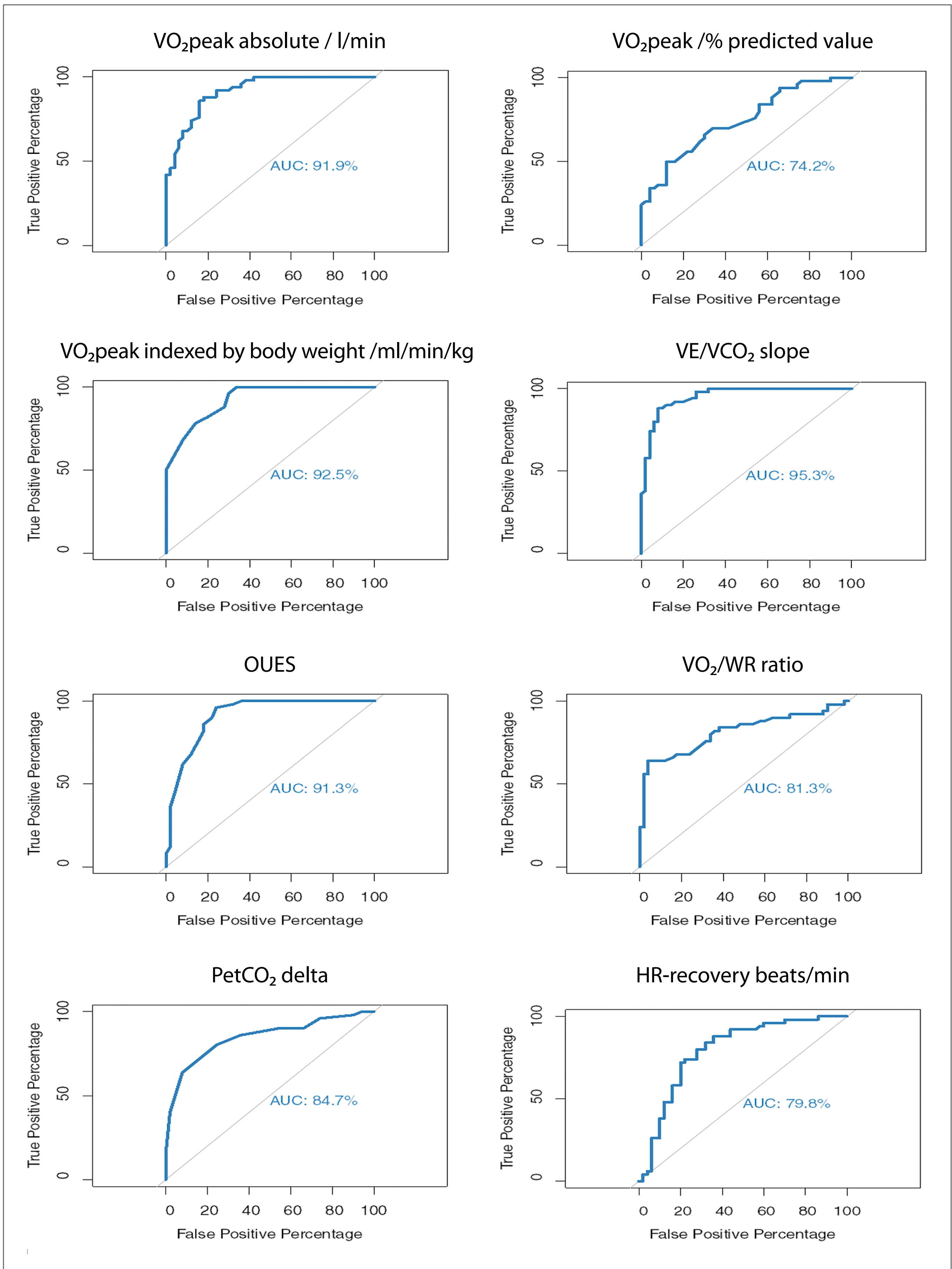

Figure 1: AUC (area under the curve) of the eight reliable parameters

Table 1: Baseline characteristics of the population

	HFpEF		Control	
	Mean	Std	Mean	Std
Age, y	82.7	5.0	66.1	11.2
BMI, kg/m^2	27.3	4.4	27.2	4.0
History of arterial hypertension	96 %		72%	
History of diabetes mellitus	24 %		10 %	
CKD, GFR < 60 ml/min	48 %		8 %	
History of atrial fibrillation	70 %		20 %	
Atrial fibrillation at the time of examination	40 %		0 %	

Table 2: Results of echocardiography

	HFpEF		Control		t-tTest
	Mean	Std	Mean	Std	p
Left atrial size, ml/m^2	53.7	19.7	26.5	10.8	< 0.0001
E/E´	12.2	4.6	7.1	1.9	< 0.0001
Estimated PA pressure, mmHg	43.1	10.9	32.0	5.5	< 0.0001
EF %	57	6,5	61	5.8	0.002

Table 3: Results of the unpaired t-test

	HFpEF		Control		t-test
	Mean	Std	Mean	Std	p
VO_2 peak, l/min	1.04	0.27	1.87	0.55	< 0.0001
VO_2peak % predicted	79.78	18.89	98.82	21.04	< 0.0001
VO_2peak, ml/min/kg	13.16	4.14	22.16	4.14	< 0.0001
VO_2 % predicted at VT1	52.7	13.75	53.54	14.71	0.7686
VE/VCO_2 slope	40.8	6.5	28.83	4.13	< 0.0001
VO_2/HR, ml/min	10.26	1.28	13.66	3.46	< 0.0001
VO_2/HR % predicted	52.7	13.75	53.54	13.75	0.1717
OUES	1.28	0.33	2.27	0.65	< 0.0001
VO_2/WR ratio, ml/min/W	7.57	2.48	10.09	1.99	< 0.0001
$PetCO_2$, mmHg	28.92	4.0	31.56	2.95	0.00031
$PetCO_2$ delta, mmHg	3.84	2.57	7.5	2.53	< 0.0001
HR-recovery, beats/min	-5.6	4.17	-11.63	5.96	< 0.0001
NT-proBNP, pg/ml	2234	2117	110	118	< 0.0001

Table 2 shows the mean values and their standard deviation for the HFpEF and control groups for the selected parameters of the echocardiography. These results showed typical values for patients with and without the diagnosis of HFpEF.

Table 3 shows the mean values and their standard deviation for the HFpEF and control groups for the selected parameters of the CPET which are described in the literature as typically affected in patients with heart failure [12, 14]. We compared these parameters between patients with HFpEF and the control group by performing an unpaired t-test, the results of which are shown in the rightmost column. Additionally, we compared the NT-proBNP values of both groups. Ten of the twelve investigated parameters were significantly different between the HFpEF patients and the control group.

Additionally, we performed ROC-curve analysis of the parameter with the highest accuracy, shown in Figure 1. We selected the parameters VO_2peak indexed by body weight, the VE/VCO_2 slope, OUES, the VO_2/WR ratio and $PetCO_2$ delta.

For the discrimination between HFpEF patients and patients without heart failure we evaluated the thresholds of the different parameters. First, we considered the known thresholds described in the literature. Additionally, we performed a logistic regression analysis of each parameter using the inflection point, the point where the curve crosses the value 0.5 of the ordinate, to fit the best threshold shown in Figure 2. Finally, we performed a ROC curve analysis with different thresholds and estimated the best value for the AUC. The aim of choosing a threshold was to find a value with good discrimination but also according to the values described in the literature.

Because oxygen uptake is one of the most important parameters with high prognostic power, we examined VO_2peak, VO_2peak as a percentage of the predicted value and VO_2peak indexed by body weight. The ROC curve analysis revealed that the VO_2peak indexed by body weight had the best AUC value. Because VO_2peak depends on sex, age, fitness level, height and weight we selected VO_2peak indexed by body weight for the score. A value above 20 ml/min/kg is unlikely for patients with heart failure, so we selected this value as the threshold [21].

The VE/VCO_2-slope was selected as the second parameter because of its high specificity for heart failure. A value less than 30 nearly excludes heart failure. However, increased values have a low sensitivity and are not specific for a cardiac limitation [22].

OUES typically changes in patients with heart failure. We chose 1.6 as the threshold. The threshold in the literature is not consistently determined [6, 17]. We selected this threshold after first performing a logistic regression analysis and using the location parameter. Second, we chose thresholds nearby and performed ROC curve analysis.

Table 4: Point system for the different parameters included in the score: a score ≥ 3 indicates HFpEF and a score of 0–2 indicates no heart failure.

Parameter	Definition	Points
VO_2peak indexed by body weight	< 20 ml/min/kg	1
VE/VCO_2 slope	> 30	1
VO_2/WR ratio	< 8 ml/min/W	1
OUES	≤ 1.6	1
$PetCO_2$ delta	≤ 4 mmHg	1

Table 5: Point system including NT-proBNP: a score ≥ 4 indicates HFpEF, 0–3 indicates no heart failure.

Parameter	Definition	Points
VO_2peak indexed by body weight	< 20 ml/min/kg	1
VE/VCO_2 slope	> 30	1
VO_2/WR ratio	< 8 ml/min/W	1
OUES	≤ 1.6	1
$PetCO_2$ delta	≤ 4 mmHg	1
NT-proBNP	≥ 300 pg/ml	1

A decreased VO_2/WR-ratio is a sign of impaired cardiac function. The VO_2/WR ratio is useful for differentiating between cardiac and pulmonary diseases. The threshold varies in the literature. We selected a threshold of 8 ml/min/W because patients with heart failure often have a value under 8 ml/min/W [20] and the inflection point of the regression analysis was nearby.

An altered $PetCO_2$ kinetic reflects heart failure. An increase of 3 or more mmHg during exercise is described as normal [14, 21]. We chose a threshold of 4 mmHg or less for $PetCO_2$ delta by performing various ROC curve analyses.

HFpEF-CPET score

The HFpEF-CPET score was generated by assigning one point for each of the following criteria: VO_2 indexed by body weight < 20 ml/min/kg, VE/VCO2 slope > 30, VO_2/WR-ratio < 8 ml/min/watt, OUES ≤ 1,6 and $PetCO_2$ delta ≤ 4 mmHg (see also Table 4). The total score ranges from 0 to 5 points. A score of 3–5 points indicates a positive diagnosis of HFpEF, and a score of 0–2 points indicates a negative diagnosis of HFpEF. In our patient population, the AUC in the ROC curve analysis was 0,976, yielding a sensitivity of 91% and a specificity of 96% for diagnosing HFpEF.

An improvement in the AUC was achieved by combining of the previous parameters with the results of the NT-proBNP measurements. We selected a threshold of 300 pg/ml for all patients for simplicity. This threshold was proposed in the 2021 ESC guidelines for patients with acute heart failure [7]. If the NT-proBNP value is evaluated, a score of 0–3 points indicates a negative diagnosis of HFpEF. A score of 4–6 points indicates a positive diagnosis of HFpEF and an AUC value of 0.99, a sensitivity of 100%, and a specificity of 96% are achieved (Table 5).

Discussion

The CPET is a unique test used to evaluate the capacity of a patient and to assess exercise intolerance and dyspnoea. However, to discriminate between heart failure and other causes of exercise intolerance, a single parameter of the CPET is not specific enough. Previous investigations revealed a high probability of heart failure if the VO_2peak was reduced and the VE/VCO_2 slope was elevated. Neither parameter is specific for cardiac limitation, and with intermediate results further investigations are needed [9]. In the previous sections we aimed to create a score to confirm the diagnosis of HFpEF by combining several parameters that are affected by cardiac limitations.

We compared twelve parameters of the CPET in patients with HFpEF with a control group with no evidence of heart failure. To create the score, we wanted to combine no more than six parameters to keep the score as simple as possible. We selected the VO_2peak indexed by body weight, the VE/VCO_2 slope, the VO_2/WR ratio, the OUES and the increase in $PetCO_2$ during exercise because these parameters yield the best results by performing ROC-curve analysis and are covering different aspects of CPET.

Peak oxygen consumption and ventilatory efficiency measured by VE/VCO_2-slope are the most important parameters for evaluating the reasons of exercise intolerance. Reduced OUES and aerobic capacity measured by the VO_2/WR ratio are relatively specific for heart failure. Low $PetCO_2$ delta reflects low CO_2-production and is reflected in heart failure but

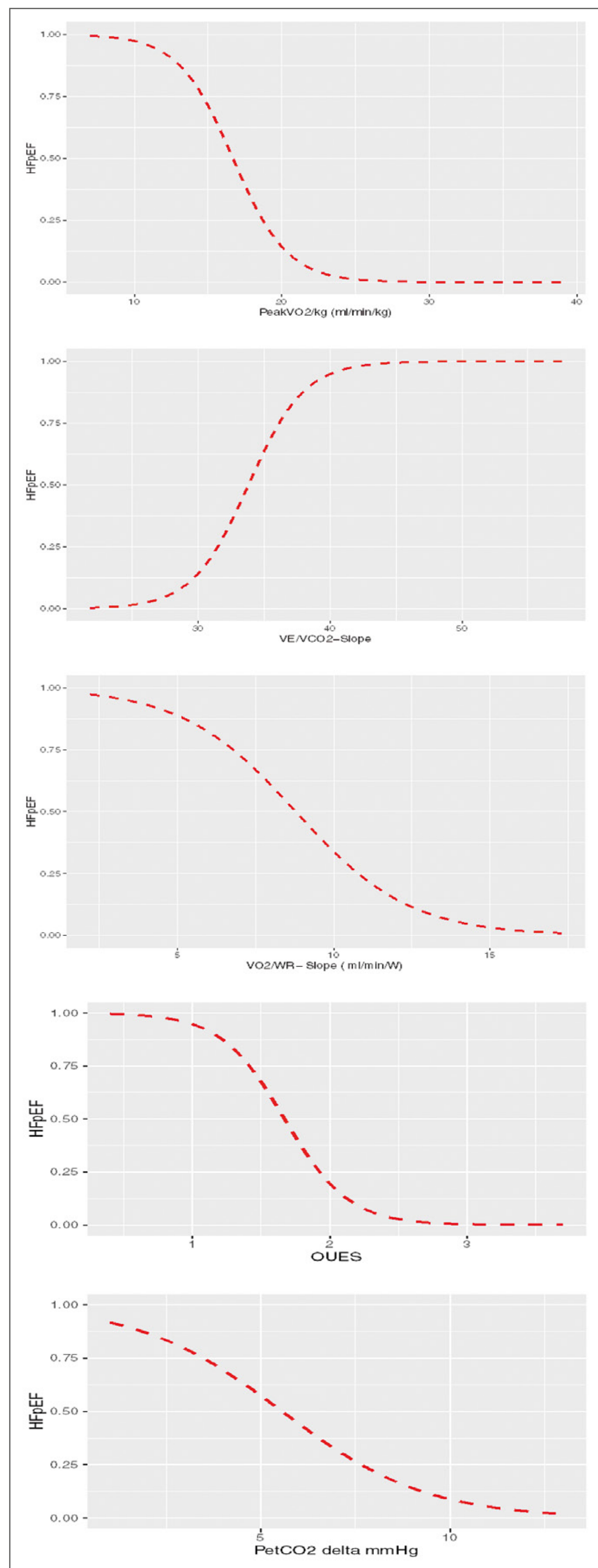

Figure 2: Logistic regression of the five parameters of the HFpEF-CPET score

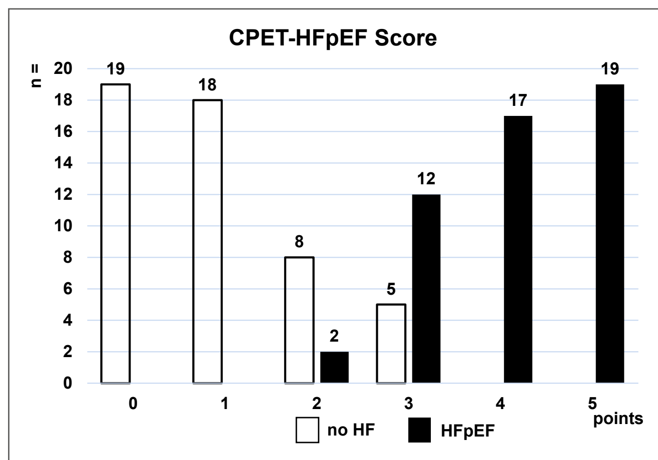

Figure 3: Results of the application of the HFpEF-CPET score to our patient-population, with white bars for patients without heart failure and black bars for patients with HFpEF

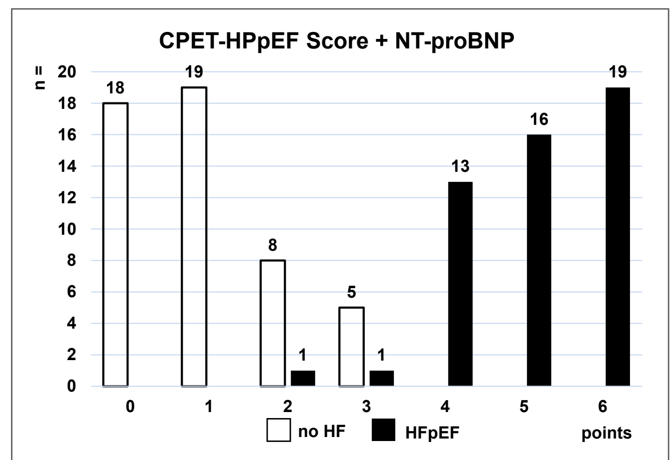

Figure 4: Results of the application of the HFpEF-CPET score in combination with NT-proBNP measurements to our patient-population, with white bars for patients without heart failure and black bars for patients with HFpEF

also in lung diseases. The thresholds for differentiating between HFpEF and no evidence of heart failure were selected by considering the thresholds mentioned in the literature, the inflection points, logistic regression analysis and ROC curve analysis. A score with these five parameters obtained a high sensitivity and specificity for the diagnosis of HFpEF in our patient population. By adding the value of NT-proBNP we achieved an improvement in sensitivity, while the specificity remained the same. Compared with the two noninvasive scoring systems for diagnosing HFpEF, the H2FPEF score and the HFA-HPFF score [23], the CPET-HFpEF score clearly improve the diagnostic power.

Churchill and Li demonstrated good overall performance of the HFA-PEFF algorithm and the H2FPEF score in patients, who underwent cardiopulmonary exercise testing with invasive hemodynamic monitoring. But they highlighted potential misclassification, particularly at low scores. While the full HFA-PEFF algorithm achieved a sensitivity and specificity of 72% and 91%, respectively, the H2FPEF score lead to a sensitivity of 31% and a specificity of 92% [24].

We abstained from integrating the O_2-pulse, oxygen uptake at the first ventilatory threshold and heart rate recovery into the score for several reasons. Because the O_2 pulse is influenced by the use of betablockers and we did not interrupt the medication before the CPET, its inclusion could influence the results. Additionally, we found no significant difference in the predicted O_2 pulse between the two groups making it unsuitable for scoring. These results may have been influenced by the different age of both groups. The oxygen uptake at the first ventilatory threshold (VO_2/VT1%) was not significantly different between the two groups. Although heart rate recovery was significantly different, including it in the score had no additional benefit discriminating between HFpEF patients and non-HFpEF patients, as determined by ROC curve analysis.

Limitations

The score was developed for patients with unexplained dyspnoea or exercise intolerance and a preserved ejection fraction on echocardiography to differentiate between HFpEF and no evidence of heart failure. The diagnosis of HFpEF was not confirmed by invasive haemodynamic assessment with right heart catheterization, but we used the maximal score of HFA-PEFF algorithms for the diagnosis of HFpEF. Additionally, this was a single-center study, and the sample size was relatively small.

Finally, the control group differed in terms of age and some comorbidities. For example, patients with atrial fibrillation were significantly more common in the HFpEF group, but atrial fibrillation is a significant concomitant phenomenon of HFpEF. Probably this score will also improve the diagnosis of HFrEF and HFmrEF, but this was not subject of the study.

Conclusion

The gold standard for diagnosing HFpEF is the invasive measurement of elevated filling pressures. With the CPET it is possible to verify typical signs of heart failure, such as exercise intolerance and dyspnoea and objective parameters of impaired cardiac function in just one comprehensive examination. The HFpEF-CPET score is a test that makes the diagnosis of HFpEF very accurate and additionally provides information about the prognosis and fitness level of the patient. The combination of five parameters of the CPET has very high diagnostic value and discriminates well between patients with HFpEF and patients without heart failure. Furthermore, in combination with NT-proBNP the diagnostic power can be further increased.

Conflict of Interest

The authors declare that they have no conflict of interest.

References:

1. Istratoaie S, Gargani L, Popescu BA, Thomas L, Voigt JU, Donal E. How to diagnose heart failure with preserved ejection fraction. Eur Heart J Cardiovasc Imaging 2024; 25: 1505–16.

2. von Haehling S, Assmus B, Bekfani T, Dworatzek E, Edelmann F, Hashemi D, et al. Heart failure with preserved ejection fraction: diagnosis, risk assessment, and treatment. Clin Res Cardiol 2024; 113: 1287–305.

3. Borlaug BA, Sharma K, Shah SJ, Ho JE. Heart failure with preserved ejection fraction: JACC Scientific Statement. J Am Coll Cardiol 2023; 81: 1810–34.

4. Pieske B, Tschöpe C, de Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J 2019; 40: 3297–317.

5. Reddy YNV, Carter RE, Obokata M, Redfield MM, Borlaug BA. A simple, evidence-based

approach to help guide diagnosis of heart failure with preserved ejection fraction. Circulation 2018; 138: 861–70.

6. Agdamag AC, Van Iterson EH, Tang WHW, Finet JE. Prognostic role of metabolic exercise testing in heart failure. J Clin Med 2023; 12: 4438.

7. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021; 42: 3599–726. Erratum in: Eur Heart J 2021; 42: 4901.

8. Guazzi M, Wilhelm M, Halle M, Van Craenenbroeck E, Kemps H, de Boer RA, et al. Exercise testing in heart failure with preserved ejection fraction: an appraisal through diagnosis, pathophysiology and therapy – a clinical consensus statement of the Heart Failure Association and European Association of Preventive Cardiology of the European Society of Cardiology. Eur J Heart Fail 2022; 24: 1327–45.

9. Reddy YNV, Olson TP, Obokata M, Melenovsky V, Borlaug BA. Hemodynamic correlates and diagnostic role of cardiopulmonary exercise testing in heart failure with preserved ejection fraction. JACC Heart Fail 2018; 6: 665–75.

10. Li S, Zhu X, Zhang Y, Li F, Guo S. Validation of heart failure algorithm for diagnosing heart failure with preserved ejection fraction: a meta-analysis. ESC Heart Fail 2023; 10: 2225–35.

11. Arena R, Myers J, Abella J, Peberdy MA, Bensimhon D, Chase P, Guazzi M. Development of a ventilatory classification system in patients with heart failure. Circulation 2007; 115: 2410–7.

12. Arena R, Sietsema KE. Cardiopulmonary exercise testing in the clinical evaluation of patients with heart and lung disease. Circulation 2011; 123: 668–80.

13. Guazzi M, Bandera F, Ozemek C, Systrom D, Arena R. Cardiopulmonary exercise testing: what is its value? J Am Coll Cardiol 2017; 70: 1618–36.

14. Herdy AH, Ritt LE, Stein R, Araújo CG, Milani M, Meneghelo RS, et al. Cardiopulmonary exercise test: background, applicability and interpretation. Arq Bras Cardiol 2016; 107: 467–81.

15. Adachi H. Cardiopulmonary exercise test. Int Heart J 2017; 58: 654–65.

16. Forman DE, Myers J, Lavie CJ, Guazzi M, Celli B, Arena R. Cardiopulmonary exercise testing: relevant but underused. Postgrad Med 2010; 122: 68–86.

17. Davies LC, Wensel R, Georgiadou P, Cicoira M, Coats AJ, Piepoli MF, Francis DP. Enhanced prognostic value from cardiopulmonary exercise testing in chronic heart failure by non-linear analysis: oxygen uptake efficiency slope. Eur Heart J 2006; 27: 684–90.

18. Malhotra R, Bakken K, D'Elia E, Lewis GD. Cardiopulmonary exercise testing in heart failure. JACC Heart Fail 2016; 4: 607–16.

19. Dewar A, Kass L, Stephens RCM, Tetlow N, Desai T. Heart rate recovery assessed by cardiopulmonary exercise testing in patients with cardiovascular disease: relationship with prognosis. Int J Environ Res Public Health 2023; 20: 4678.

20. Glaab T, Taube C. Practical guide to cardiopulmonary exercise testing in adults. Respir Res 2022; 23: 9.

21. Triantafyllidi H, Birmpa D, Benas D, Trivilou P, Fambri A, Iliodromitis EK. Cardiopulmonary exercise testing: the ABC for the clinical cardiologist. Cardiology 2022; 147: 62–71.

22. Andonian BJ, Hardy N, Bendelac A, Polys N, Kraus WE. Making cardiopulmonary exercise testing interpretable for clinicians. Curr Sports Med Rep 2021; 20: 545–52.

23. Amanai S, Harada T, Kagami K, Yoshida K, Kato T, Wada N, Obokata M. The H2FPEF and HFA-PEFF algorithms for predicting exercise intolerance and abnormal hemodynamics in heart failure with preserved ejection fraction. Sci Rep 2022; 12: 13.

24. Churchill TW, Li SX, Curreri L, Zern EK, Lau ES, Liu EE, et al. Evaluation of 2 existing diagnostic scores for heart failure with preserved ejection fraction against a comprehensively phenotyped cohort. Circulation 2021; 143: 289–91.

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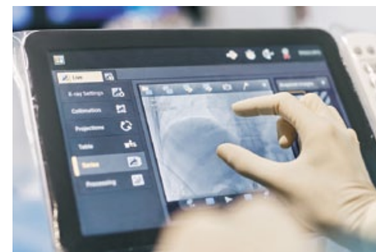

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