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CARDIOPULMONARY TEST AS A COMPONENT IN THE DIAGNOSTIC ALGORITHM FOR HEART FAILURE WITH PRESERVED LEFT VENTRICULAR EJECTION FRACTION IN PATIENTS WITH ATRIAL FIBRILLATION

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ABSTRACT

Background: *Patients with heart failure with preserved ejection fraction account for more than half of all hospitalizations because of heart failure. On the other hand, atrial fibrillation and heart failure are quite often diagnosed together and one disease influences the development of the other. Timely and accurate diagnosis of heart failure with preserved ejection fraction is the basis for effective treatment of this category of patients. In 2019, the HFA-PEFF algorithm of diagnosis heart failure with preserved ejection fraction (including patients with atrial fibrillation) was proposed. However, the algorithm implies cardiac catheterization in patients at intermediate risk, which involves certain difficulties and cannot be used in routine practice. As an alternative to cardiac catheterization in the diagnosis of heart failure with preserved ejection fraction, we proposed a noninvasive diagnostic method — cardiopulmonary test. However, the value of cardiopulmonary test technique has not been conclusively studied, especially in patients with a combination of chronic heart failure and atrial fibrillation.* ***Aim:*** *The aim of the study was to evaluate the role of the cardiopulmonary test in the diagnosis of heart failure with preserved ejection fraction in patients with atrial fibrillation.* ***Methods:*** *138 patients with atrial fibrillation were included in our study. Using HFA-PEFF algorithm (algorithm for diagnosis of heart failure with preserved left ventricular ejection fraction) all patients were initially divided into 3 groups: low probability of heart failure — 23 patients, intermediate probability — 96 and high probability — 19 patients. The stress-test allowed to precisely assess of patients at intermediate risk and finally form the groups: Group 1 without heart failure, 85 patients (61.6%); Group 2 patients with heart failure and preserved ejection fraction, 53 patients (38.4%). The next diagnostic stage was cardiopulmonary test.* ***Results:*** *During cardiopulmonary test, the anaerobic exercise threshold was 6.8 and 4.85 METs for the first and second groups, respectively ($p < 0.001$), reflecting lower exercise tolerance in the second group of patients. Analysis of variance (ANOVA) demonstrated a statistically significant increase in pro-BNP levels with a decrease in peak VO_2 ($p < 0.001$). Also, analysis of variance demonstrated a significant statistical difference with respect to systolic pulmonary artery pressure in the subgroups with severely, moderately reduced oxygen consumption and in the group with normal peak VO_2 ($p=0.01$). ROC analysis determined a peak VO_2 of 20 ml/kg/min, above which the HFA-PEFF algorithm was unlikely to detect heart failure (AUC 0.73; confidence interval 0.65–0.82; $p=0.043$; sensitivity 85%; specificity 51%).* ***Conclusion:*** *The cardiopulmonary test is a reliable instrumental non-invasive method in the diagnosis of heart failure with preserved ejection fraction.*

Keywords: *atrial fibrillation; chronic heart failure; cardiopulmonary test; ergospirometry.*

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КАРДИОПУЛЬМОНАЛЬНЫЙ ТЕСТ КАК КОМПОНЕНТ В ДИАГНОСТИЧЕСКОМ АЛГОРИТМЕ ОПРЕДЕЛЕНИЯ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ С СОХРАННОЙ ФРАКЦИЕЙ ВЫБРОСА ЛЕВОГО ЖЕЛУДОЧКА У ПАЦИЕНТОВ С ФИБРИЛЛЯЦИЕЙ ПРЕДСЕРДИЙ

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АННОТАЦИЯ

Обоснование. *На долю пациентов с сердечной недостаточностью и сохранной фракцией выброса приходится более половины всех госпитализаций по поводу сердечной недостаточности как таковой. С другой стороны, фибрилляцию предсердий и сердечную недостаточность часто диагностируют совместно, и одно заболевание влияет на развитие другого. Своевременная и точная диагностика сердечной недостаточности с сохранной фракцией выброса является основой эффективного лечения этой категории пациентов. В 2019 году Европейской ассоциацией кардиологов был предложен алгоритм HFA-PEFF по диагностике сердечной недостаточности с сохранной фракцией выброса, в том числе у пациентов с фибрилляцией предсердий. Алгоритм подразумевает также катетеризацию сердца у пациентов промежуточного риска, что сопряжено с определенными трудностями и не может использоваться в рутинной практике. В качестве альтернативы катетеризации сердца при диагностике сердечной недостаточности с сохранной фракцией выброса нами был предложен неинвазивный метод диагностики — кардиопульмональный тест, однако ценность методики окончательно не изучена, тем более у пациентов с фибрилляцией предсердий.* ***Цель исследования*** *— оценить роль кардиопульмонального тестирования в диагностике сердечной недостаточности с сохранной фракцией выброса левого желудочка у пациентов с фибрилляцией предсердий.* ***Методы.*** *В исследование включено 138 пациентов с фибрилляцией предсердий. Используя алгоритм HFA-PEFF (алгоритм диагностики сердечной недостаточности с сохранной фракцией выброса левого желудочка), все пациенты изначально были разделены на 3 группы: с низкой (n=23), умеренной (n=96) и высокой (n=19) вероятностью сердечной недостаточности. Проведение стресс-теста позволило прецизионно оценить пациентов с промежуточным риском и окончательно сформировать группы: 1-я группа — пациенты без сердечной недостаточности (n=85; 61,6%); 2-я группа — пациенты с сердечной недостаточностью и сохранной фракцией выброса (n=53; 38,4%). Следующим диагностическим этапом было проведение кардиопульмонального тестирования.* ***Результаты.*** *При проведении кардиопульмонального теста порог анаэробной нагрузки составил 6,8 и 4,85 METs для 1-й и 2-й группы соответственно (p <0,001), что отражает более низкую толерантность к физической нагрузке во 2-й группе больных. Дисперсионный анализ (ANOVA) продемонстрировал статистически значимое повышение уровня pro-BNP при снижении пикового значения VO_2 (p <0,001). Было также показано значимое статистическое различие в отношении систолического давления в легочной артерии в подгруппах с выраженным, умеренно сниженным потреблением кислорода и в группе с нормальным пиковым VO_2 (p=0,01). Проведенный ROC-анализ определил значение пикового VO_2 — 20 мл/кг в минуту, выше которого вероятность постановки диагноза сердечной недостаточности с использованием алгоритма HFA-PEFF будет маловероятной (AUC 0,73; доверительный интервал 0,65–0,82; p=0,043; чувствительность 85%; специфичность 51%).* ***Заключение.*** *Кардиопульмональный тест является надежным неинвазивным инструментальным методом диагностики сердечной недостаточности с сохранной фракцией выброса.*

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Ключевые слова: *фибрилляция предсердий; хроническая сердечная недостаточность; кардиопульмональный тест; эргоспирометрия.*

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BACKGROUND

More than half of heart failure (HF) hospitalizations are due to patients with preserved ejection fraction [1]. Atrial fibrillation (AF) and CH are often diagnosed together, and one disease can influence the development of the other [2–4].

A timely and accurate diagnosis of HF with preserved ejection fraction is crucial for effective treatment of this patient population. In 2019, the Heart Failure Association of the European Society of Cardiology (HFA/ESC) proposed an algorithm for diagnosing HF, which is also applicable to patients with AF [5].

The use of the "new" diagnostic algorithm, rather than the H2FPEF algorithm [6], enables accurate diagnosis of HF with preserved ejection fraction. However, the algorithm requires cardiac catheterization in intermediate-risk patients, which presents certain challenges and is unsuitable for routine use. As an alternative to cardiac catheterization for diagnosing HF with preserved ejection fraction, we propose cardiopulmonary testing (ergospirometry), a noninvasive diagnostic method.

Ergospirometry, also called cardiopulmonary test, is a stress test that evaluates the reaction and interaction of the cardiovascular and respiratory systems and the metabolic response of the body to physical exercise. Gas exchange parameters, such as oxygen consumption, carbon dioxide release, and minute ventilation, are monitored during the test. Additionally, the patient's well-being, blood pressure, and electrocardiogram (ECG) are monitored [7]. The 2019 ESC guidelines state that a decrease in peak oxygen consumption (VO_2) <20 mL/kg per minute and/or an increase in minute ventilation to volume of CO_2 extracted (VE/VCO_2) >30 are predictors of high risk and confirm HF [5].

The value of the cardiopulmonary test has not been definitively studied [5, 8], especially in patients with HF combined with AF. In our study, we evaluated the cardiopulmonary test as a component in the diagnostic algorithm for determining HF with preserved ejection fraction in patients with AF and its prognostic role in cardiac surgery practice.

This study aimed to evaluate the role of cardiopulmonary testing in the diagnosis of HF with preserved left ventricular ejection fraction in patients with AF.

METHODS

Study design

A nonrandomized, uncontrolled, single-center pilot study was conducted prospectively.

Eligibility criteria

The inclusion criteria were an AF diagnosis, patient age over 18 years, normal serum thyroid hormone levels, and preserved left ventricular ejection fraction.

The inclusion criteria excluded patients who refused to participate, were under 18 years old, had a reduced left ventricular ejection fraction according to ECHO-CG, had systemic inflammatory diseases of connective tissue (such as rheumatoid arthritis or systemic lupus erythematosus), had a malignant oncological process, or had musculoskeletal diseases that impaired their self-care.

The exclusion criteria included chronic infectious processes, contraindications to anticoagulant therapy, thyroid disease accompanied by hypo- or hyperthyroidism, and thrombosis of the left atrial appendage.

Settings

The study involved 138 patients with persistent AF and preserved left ventricular ejection fraction. All participants provided written consent to participate in the study. This study was conducted at the Federal Scientific and Clinical Center for Specialized Medical Care and Medical Technologies of FMBA of Russia.

Duration of the study

The study was conducted from 2021 to 2022.

Description of the medical intervention

Table 1 presents demographic characteristics. Patients diagnosed with HF were older than those in group 1. The other demographic characteristics were comparable between the groups.

Table 2 shows the clinical characteristics of the patients. All patients were diagnosed with AF.

Upon admission to the hospital, all patients underwent laboratory and instrumental investigations, including general and biochemical blood tests, N-terminal brain prohormone natriuretic peptide (NT pro-BNP), chest X-ray, electrocardiogram (ECG), transthoracic echocardiography (Table 3), and cardiopulmonary testing. If required, transesophageal echocardiography, coronarography, and other investigative methods were performed.

The next step in the diagnosis was cardiopulmonary exercise testing. A treadmill was used with changes in running speed and a track incline according to the Bruce protocol (Table 4) [9]. Criteria for discontinuing exercise testing include angina or chest pain, ischemia or arrhythmia on ECG, systolic blood pressure >250 mm Hg or diastolic blood pressure >120 mm Hg, decrease in blood pressure >20 mmHg from the highest value during testing, oxygen desaturation <80%, weakness, dizziness, impaired consciousness, or signs of respiratory failure [11, 11].

Ethical review

The study received approval from the local ethical committee of the Federal Scientific and Clinical Center for Specialized Medical Care and Medical Technologies of FMBA of Russia, as evidenced by extracts from protocols no. 9, 2021, and no. 8, 2022.

Table 1

Demographic characteristics of patients

Index	Group 1 (*n*=85)	Group 2 (*n*=53)	*p*
Age, years	**59** (55; 65)	**65** (62; 69.3)	**<0.01**
Gender, male/female*	67 (78.8%) / 18 (21.2%)	37 (69.8%) / 16 (30.2%)	>0.05
Body mass index, kg/m^2	30 (27.5; 33)	29 (28; 32)	>0.05
Body surface area, m^2	2.08 (1.93; 2.23)	2.04 (1.86; 2.18)	>0.05

Note: Quantitative data are presented as Me (Q_1; Q_3), where Me is median, Q_1 and Q_3 are lower and upper quartiles, respectively; * data are presented as absolute values (percentages). In tables 1–3, 5, indicators are highlighted in bold, when comparing which a statistically significant difference was determined.

Table 2

Clinical characteristics of patients

Index	Group 1 (*n*=85)	Group 2 (*n*=53)	*p*
History of arrhythmia, years	4 (2; 7.75)*	6 (2.75; 10)*	>0.05
Arterial hypertension, *n* (%)	65 (76.5)	44 (83)	>0.05
Postinfarction cardiosclerosis, *n* (%)	7 (8.2)	8 (15.1)	>0.05
History of percutaneous coronary intervention, *n* (%)	7 (8.2)	8 (15.1)	>0.05
Acute cerebral circulatory disorder Transient ischemic attack, *n* (%)	6 (7)	10 (18.7)	>0.05
History of thromboembolic complications, *n* (%)	-	1 (1.9)	>0.05
Chronic obstructive pulmonary disease, *n* (%)	2 (2.3)	4 (7.5)	>0.05
Brachiocephalic artery atherosclerosis, *n* (%)	13 (15.3)	9 (17)	>0.05
Atherosclerosis of the lower limb arteries, *n* (%)	3 (3.5)	6 (11.3)	>0.05
Diabetes mellitus, *n* (%)	10 (11.8)	10 (18.7)	>0.05
Kidney pathology, *n* (%)	27 (31.8)	14 (26.4)	>0.05
History of catheter ablation, *n* (%)	**36 (42.3)**	**8 (15.1)**	**<0.05**

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End of Table 2

Index	Group 1 (*n*=85)	Group 2 (*n*=53)	*p*
Atrial fibrillation form, *n* (%)			
• Paroxysmal	**78 (92.8)**	**36 (67.9)**	**<0.05**
• Persistent	7 (8.2)	5 (9.4)	>0.05
• Long persistent	-	**12 (22.6)**	**<0.05**
EHRA index, *n* (%)			
• I	**49 (57.6)**	**20 (37.7)**	**<0.05**
• II	**27 (31.8)**	**26 (49.1)**	**<0.05**
• III	9 (10.6)	7 (13.2)	>0.05
NYHA functional class, *n* (%)			
• NYHA 0	**22 (25.9)**	**5 (9.4)**	**<0.05**
• NYHA I	23 (27)	15 (28.3)	>0.05
• NYHA II	39 (45.9)	32 (60.4)	>0.05
• NYHA III	1 (1.2)	1 (1.9)	>0.05

Note: Data are presented as absolute values (percentages), *p* value was calculated by Mann–Whitney or χ2 method and Fisher exact test depending on data type; * quantitative data are presented as Me (Q_1; Q_3), where Me — median, Q_1 and Q_3 — lower and upper quartiles, respectively. EHRA — European Heart Rhythm Association atrial fibrillation symptom rating scale; NYHA — New York classification of functional class of heart failure.

Table 3

Data of instrumental and laboratory examination methods

Echocardiography and NT-proBNP	Group 1 (*n*=85)	Group 2 (*n*=53)	*p*
LV ejection fraction, %	60 (56.5; 63)	60 (57; 63)	>0.05
LA Indexed volume, mL/m^2	**31 (26; 34)**	**40 (34.8; 46.6)**	**<0.001**
LV end-diastolic volume, mL	104 (90; 121)	100.5 (85.8; 121.8)	>0.05
LV end-systolic volume, mL	37 (32; 45)	36.5 (31.8; 49.5)	>0.05
LV end-diastolic dimension, cm	5 (4.7; 5.3)	5 (4.6; 5.23)	>0.05
LV end-systolic dimension, cm	3.2 (2.8; 3.45)	3.4 (2.9; 3.6)	>0.05
LV myocardial mass index, g/m^2	79 (66.5; 92.5)	80 (66; 90)	>0.05
Pressure in the pulmonary arteries, mmHg	**25 (20; 29.5)**	**34 (26.8; 43.3)**	**<0.001**
E/e′, cm/sec	9.5 (8; 11.9)	10 (8.5; 14)	>0.05
Indexed right atrial volume, mL/m^2	**22 (19; 26)**	**29.5 (23; 36.6)**	**<0.001**
TAPSE, cm	**2 (1.8; 2.1)**	**1.78 (1.6; 2)**	**0.027**
NT-proBNP, pg/mL	**102.6 (68.12; 208.6)**	**483 (264.8; 794.1)**	**<0.001**

Note: Quantitative data are presented as Me (Q_1; Q_3), where Me is the median, Q_1 and Q_3 are the lower and upper quartiles, respectively; p-value between groups calculated by the Mann–Whitney method. LV — left ventricle; LA — left atrium; E/e′ — ratio of peak velocities of early transmitral blood flow and early diastolic movement of the mitral ring; TAPSE — tricuspid annular plane systolic excursion; NT-proBNP — N-terminal brain prohormone natriuretic peptide.

Table 4

Bruce protocol for cardiopulmonary testing

Step, no.	Speed, km/h	Lift angle, %	Duration, min
1	2.7	10	3
2	4.0	12	3
3	5.5	14	3
4	6.8	16	3
5	8.0	18	3
6	8.9	20	3
7	9.7	22	3

Statistical analysis

The SPSS 28.0.0.0.0 software package (IBM SPSS Statistics, Chicago, IL, USA) was used for data analysis. Quantitative data were presented as median (Me) and quartiles (25%; 75%), and categorical data were presented as absolute number (n) and proportion (%). Analysis of variance (ANOVA) was performed. The Mann–Whitney U test was used to compare two independent groups, whereas the Kruskal–Wallis test was used for three independent groups. For categorical features, the $\chi 2$ test with Yates correction and Fisher's exact test were used. The discriminatory ability and reliability of peak oxygen consumption in determining HF, as well as the sensitivity and specificity of this factor, was evaluated using receiver operating characteristic (ROC) analysis. Statistical significance was established at $p < 0.05$.

RESULTS

Objects (participants) of the study

The study included 138 patients with AF who received FMBA treatment in 2021. The majority of patients had a history of surgical intervention at our clinic and underwent repeated postoperative examination and health monitoring. All patients were diagnosed with AF and had a normal left ventricular ejection fraction. The HFA-PEFF algorithm (Heart Failure Association Pretest assessment, Echocardiography and natriuretic peptide, Functional testing, Final etiology) was used to initially divide the patients into three groups based on their probability of developing HF: low (*n*=23), moderate (*n*=96), and high (*n*=19). An additional stress test was conducted to accurately evaluate patients with intermediate risk (2–4 points) and finalize the groups. Group 1 comprised 85 patients without HF (61.6%), and group 2 involved 53 patients with HG and preserved ejection fraction (38.4%) (Fig. 1).

Main results of the study

Clinical data analysis showed that patients in group 2 (with HF) were generally older than those in group 1. Additionally, this group had a higher number of patients with persistent and long-term persistent AF, a longer history of AF, and a higher frequency of

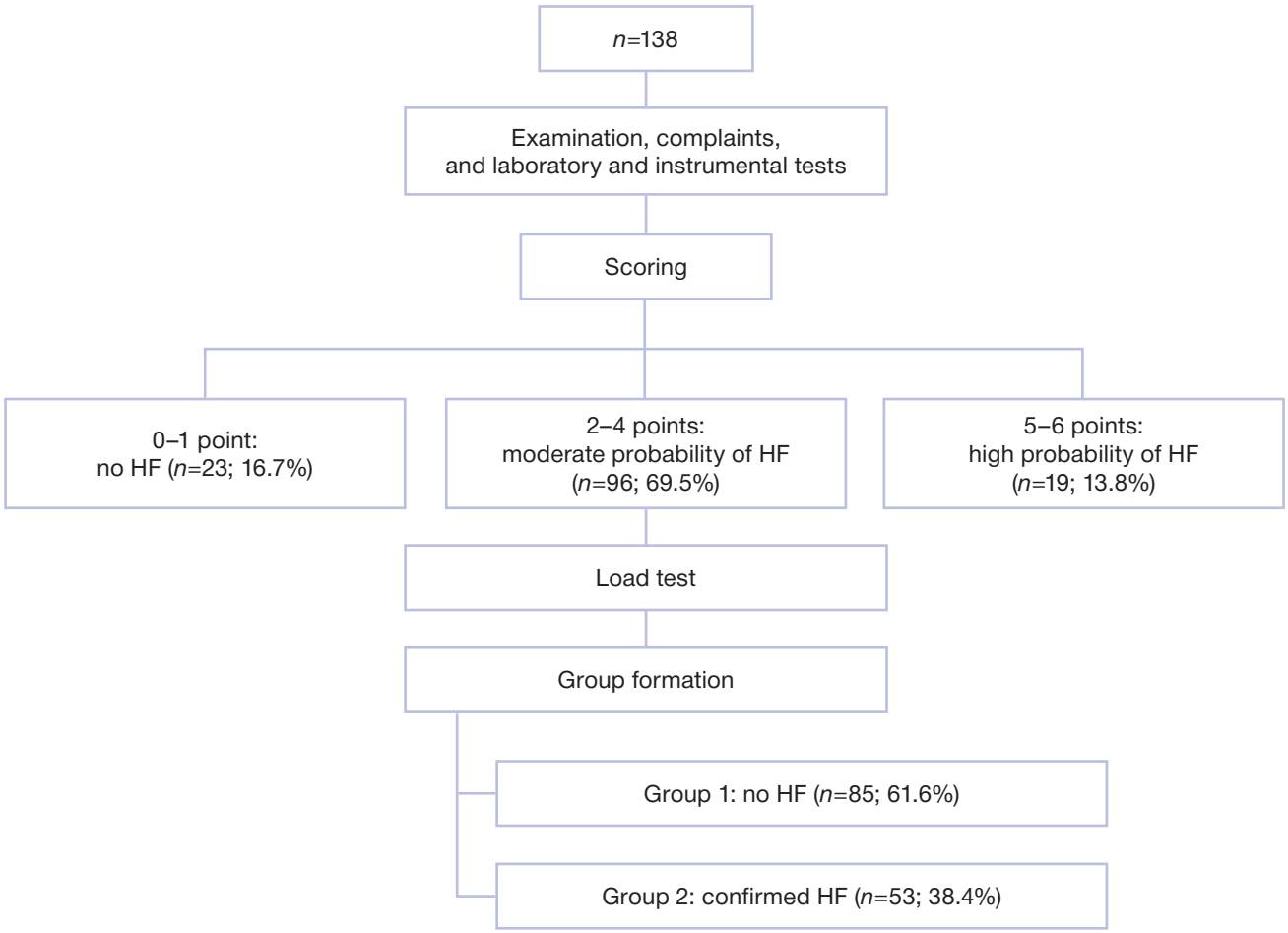

Fig. 1. Diagnostic algorithm of heart failure with preserved ejection fraction in patients with atrial fibrillation. HF — heart failure.

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dyspnea complaints during minimal and moderate physical activity (79.2% vs. 43.5% in group 1, p <0.05).

When evaluating laboratory and instrumental investigations, most patients in group 2 were found to have atriomegaly of various degrees of severity and pulmonary hypertension.

Furthermore, tricuspid annular plane systolic excursion (TAPSE), which indirectly indicates right ventricular contractility, was diagnosed below 1.7 in 11.8% and 24.5% of patients in groups 1 and 2, respectively (p <0.05). Additionally, the NT-proBNP level was significantly higher in group 2 with a median of 483 pg/mL compared with 102.6 pg/mL in group 1.

Table 5 shows statistically significant differences between the groups for each indicator of the cardiopulmonary test. Remarkably, group 2 reached the maximum threshold of anaerobic load at a lower load than group 1: 4.85 vs. 6.8 METs (metabolic equivalents), respectively (p <0.001), indicating a lower exercise tolerance.

Moreover, several calculations were performed on the entire patient sample. The patients were divided into three subgroups based on their peak oxygen consumption using ANOVA. Group 1 consisted of patients with peak VO_2 levels <17 ml/kg /min, group 2 included patients with levels between 17 and 20 mL/kg /min, and group 3 included patients with levels >20 mL/kg /min, which is considered normal (Table 6). We analyzed the works of our foreign colleagues [8] and adopted their division into ranks, while considering the presence of AF in all patients.

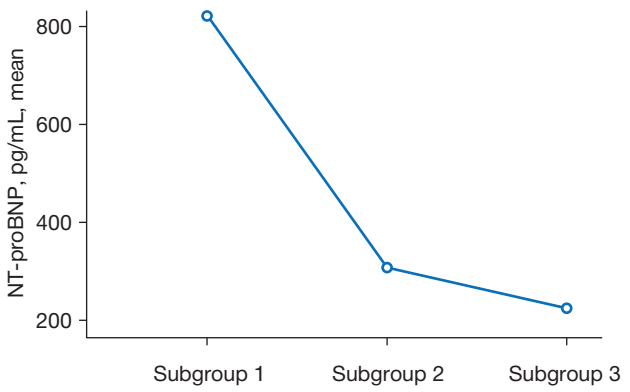

Fig. 2. Relationship between peak oxygen consumption and NT-proBNP levels (mean values) (p <0,001). NT-proBNP — N-terminal brain prohormone natriuretic peptide; VO_2 — oxygen consumption.

Figure 2 shows that the level of NT-proBNP significantly increases as peak VO_2 decreases (p <0.001). This means that the more pronounced the CH phenomena, the more severe the metabolic disorders in the patient's body and the greater the decrease in peak oxygen consumption. In contrast, the patients in the second group (oxygen consumption from 17 to

Table 5

Results of the cardiopulmonary test in the studied groups

Index	Group 1 (n=85)	Group 2 (n=53)	p
VO_2 peak, mL/kg / min	**24.79 (21.72; 29.32)***	**16.86 (14.81; 19.83)***	**<0.001**
VE/VCO_2	**30.4 (27.9; 33)***	**35.5 (31.1; 39.6)***	**<0.001**
Anaerobic metabolic threshold: maximum anaerobic exercise limit, METs	**6.8 (6.2; 7.95)***	**4.85 (4.18; 5.6)***	**<0.001**
Change in both indices in one patient (VO_2; VE/VCO_2), n (%)	5 (5.9)	37 (69.8)	**<0.001**

Note: p-value between groups calculated by Mann–Whitney method or χ2 and Fisher›s exact test depending on the type of data; * quantitative data are presented as Me (Q_1; Q_3), where Me is the median, Q_1 and Q_3 are the lower and upper quartiles, respectively; VO_2 — oxygen consumption; VE/VCO_2 — minute ventilation/carbon dioxide production.

Table 6

Analysis of variance: Testing of significance differences between VO_2 peak and pro-BNP

VO_2 peak, mL/kg / min	Number of patients, n	pro-BNP, pg/mL		
		25th	50th (median)	75th
Subgroup 1 (<17)	27	271.80	488.30*	1368.75
Subgroup 2 (17–20)	21	102.06	231.45	459.60
Subgroup 3 (>20)	90	72.54	129.70	285.55

Note: * With a decrease in O_2 consumption (1 subgroup). the level of NT-proBNP was significantly increased in relation to 2 and 3 subgroups. VO_2 — oxygen consumption; NT-proBNP — N-terminal brain prohormone natriuretic peptide.

Table 7

Analysis of variance: testing the significance of differences between VO_2 peak and pulmonary artery pressure

VO_2 peak, mL/kg / min	Number of patients, *n*	Pressure in the PA, mmHg		
		25th	50th (median)	75th
Subgroup 1 (<17)	27	29.0	34.0*	43.5
Subgroup 2 (17–20)	21	21.25	28.0	40.0
Subgroup 3 (>20)	90	20.0	25.5	30.0

Note: * In the 1st subgroup the pressure in the pulmonary arteries was significantly higher in relation to the 2nd and 3rd subgroups of patients. VO_2 — oxygen consumption; PA — pulmonary arteries.

20 mL/kg per minute) showed a moderate increase in NT-proBNP (median 231.45 pg/mL). According to ESC recommendations, this level is acceptable for patients with AF and does not always indicate HF [12]. However, 13 patients with confirmed HF were included in this group of variance analysis (i.e., VO_2 peak value was 17–20 mL/kg /min).

ANOVA showed a statistically significant difference (p=0.01) in pulmonary artery systolic pressure between the groups with markedly and moderately reduced oxygen consumption and the group with normal peak VO_2 (Table 7). In the group with reduced peak oxygen consumption <17 mL/kg per minute, pulmonary artery pressure was significantly higher in both persistent and paroxysmal forms of AF (Fig. 3).

DISCUSSION

The ANOVA showed that peak oxygen consumption decreases as the NT-proBNP level and pressure in the pulmonary artery system increase. The pathognomonic sign of diastolic dysfunction is an increase in pressure in the left atrium. As HF progresses, there is a decrease in tolerance to physical load, which is manifested by an increase in NT-proBNP levels in laboratory tests and an increase in pulmonary artery pressure in instrumental tests. This decrease in tolerance leads to unsatisfactory results in cardiopulmonary testing. The data obtained reveal that ergospirometry is a reliable diagnostic method for HF with preserved ejection fraction and are feasible in patients with AF.

ROC analysis showed that a peak VO_2 >20 mL/kg per minute would make a diagnosis of CH using the HFA-PEFF algorithm unlikely. Based on our calculations, the cutoff point for peak VO_2 was 20 mL/kg /min with an AUC of 0.73, a 95% confidence interval of 0.65–0.82, and a p-value of 0.043. The sensitivity was 85% and the specificity was 51% (Fig. 4).

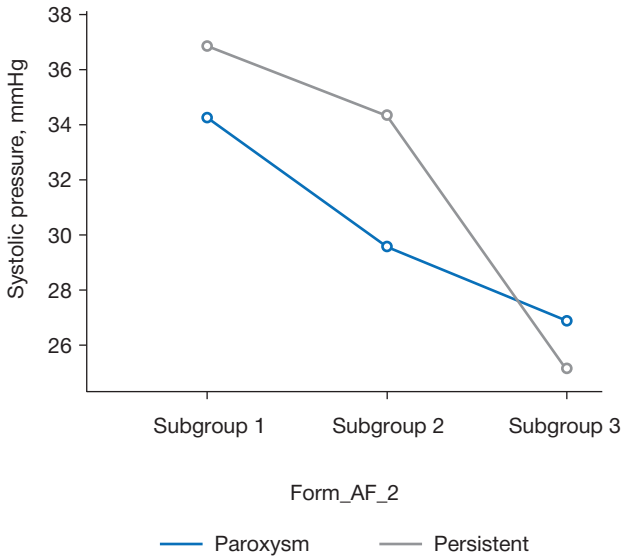

Fig. 3. Relationship between peak oxygen consumption and pulmonary artery pressure (p=0.01, Scheffe test). AF — atrial fibrillation.

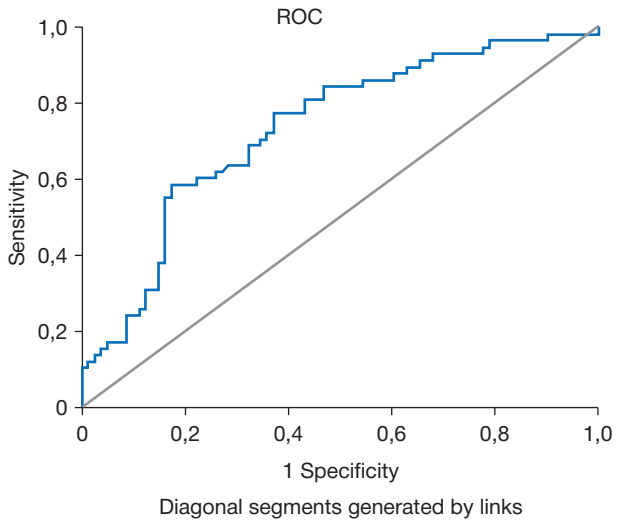

Fig. 4. Diagnosis of heart failure by peak oxygen consumption (VO_2).

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As stated in the 2019 ESC guidelines, confirmation of HF requires a reduction in peak oxygen consumption (VO_2) of <20 mL/kg /min [5].

Diagnosing HF with preserved ejection fraction can be challenging, as even recent large studies have recognized [13]. This is often because dyspnea, a common symptom of HF, may be mild and only triggered by significant exercise in patients with preserved ejection fraction and suspected HF. Additionally, dyspnea may be misattributed to other cardiovascular or pulmonary conditions or obscured by obesity [13]. Patients with HF and preserved ejection fraction have a very poor prognosis [14–16].

A recent meta-analysis found that patients with AF and reduced ejection fraction had significantly higher all-cause mortality than those with preserved myocardial contractility; however, the risk of stroke and rates of hospitalization for HF were similar in both groups [17]. Furthermore, the study showed that AF is common in patients with HF and is associated with higher mortality and repeated hospitalizations, including those for HF progression [18].

The challenge of diagnosing HF, coupled with the poor prognosis of the disease, requires an aggressive treatment approach, including surgery, for this patient population [19]. Therefore, the diagnosis of HF with preserved ejection fraction in patients with AF is a critical issue.

The HFA/ESC recommendations mention the use of ergospirometry as a method to objectively assess the decrease in physical performance and distinguish cardiac and noncardiac causes of dyspnea. However, the value of cardiopulmonary testing has not been definitively studied, especially in patients with a combination of HF and confirmed AF.

Our study found that cardiopulmonary test can diagnose HF with preserved ejection fraction in patients with AF. ANOVA revealed a significant decrease in peak VO_2 as HF progressed, which was associated with increasing pro-BNP levels and pulmonary artery pressure.

ROC analysis showed that VO_2 peak values above a certain threshold make the presence of CH in a patient unlikely. In our study, the value was 20 mL/kg /min with an AUC of 0.73, a confidence interval of 0.65–0.82, and a *p*-value of 0.043. The sensitivity was 85% and the specificity was 51%. Our foreign colleagues [5, 8] obtained similar results.

Based on the aforementioned information, we conclude that the cardiopulmonary test is a dependable diagnostic tool for HF with preserved ejection fraction. Our study successfully demonstrated the effectiveness of this method in patients with both HF and AF, which had not been previously reported. Furthermore, the method can be applied in patients with intermediate risk using the new HF diagnostic algorithm, HFA-PEFF. Based on current recommendations, intermediate-risk patients are typically subjected to cardiac probing, which may not be practical in routine clinical practice. Performing cardiopulmonary testing in this patient population can help identify the presence of HF or rule out the diagnosis.

Ergospirometry may be useful in cardiac surgery. If a patient with AF and HF has a VO_2 peak <20 mL/kg / min, it may indicate a high-risk group and warrant an aggressive surgical approach.

Therefore, we recommend modifying the HFA-PEFF algorithm for diagnosing HF in patients with AF. If intermediate risk is present, cardiopulmonary testing is warranted (Fig. 5).

CONCLUSIONS

Our study demonstrates that ergospirometry can be a reliable alternative to invasive testing and the 6-min walk test, providing valuable information for clinicians. Cardiopulmonary testing is a reliable aid in diagnosing HF in patients with preserved ejection fraction.

ADDITIONAL INFORMATION

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Authors' contribution. *A.S. Zotov* — processing and discussion of the results of the study, writing the text of the article; *E.S. Gorbacheva* — performing cardiopulmonary testing, writing the text of the article; *I.A. Mandel* — methodological support, statistical processing; *E.R. Sakharov*, *O.O. Shelest* — search and analytical work; *A.V. Troitsky*, *R.I. Khabazov* — discussion of the results of the study, general management. The authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

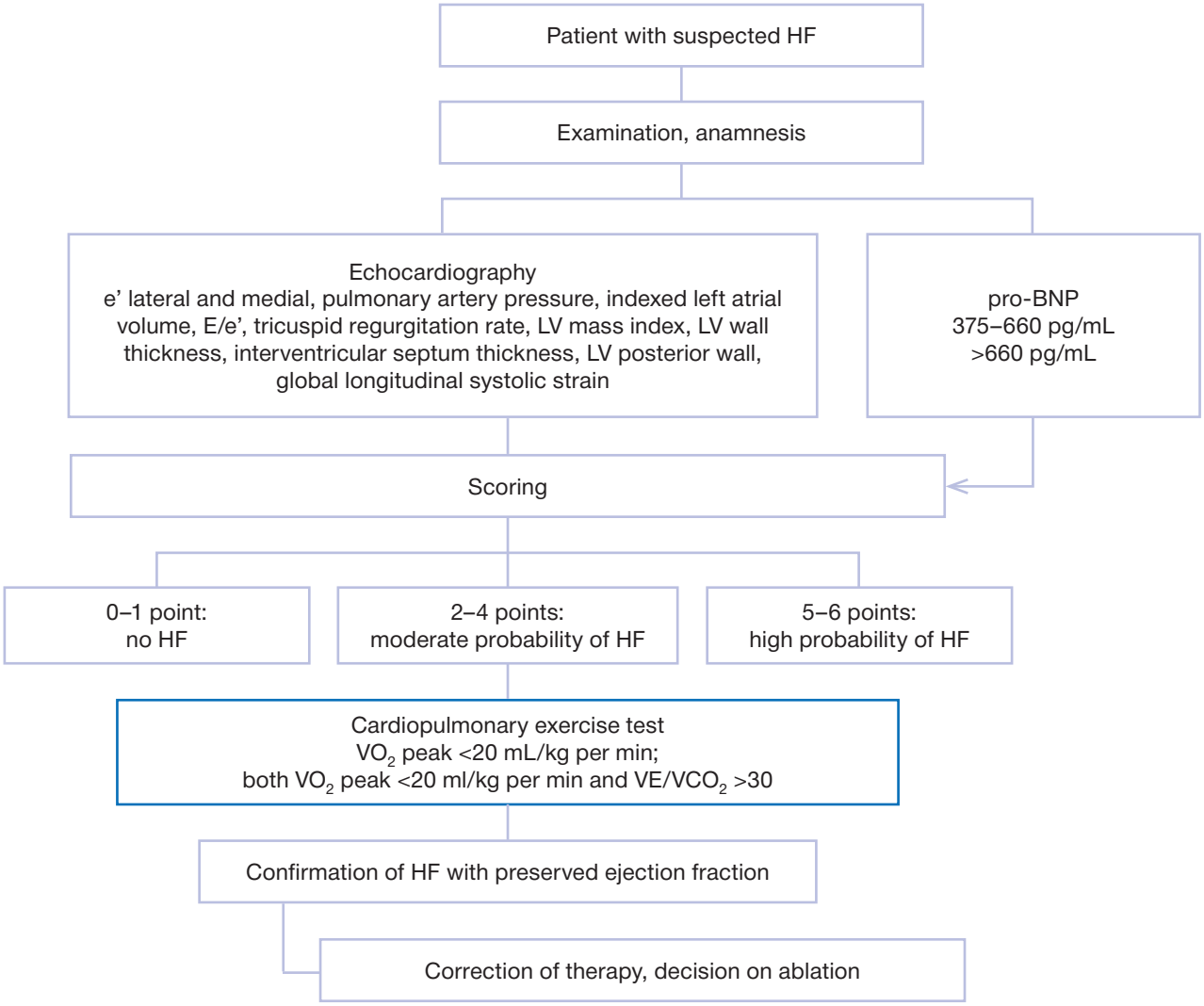

Fig. 5. Algorithm for diagnosing heart failure [5]: Use of cardiopulmonary testing to confirm heart failure in patients with atrial fibrillation. HF — heart failure; LV — left ventricle; e' — early diastolic speed of the mitral ring; E/e' — ratio of peak velocities of early transmitral blood flow and early diastolic movement of the mitral ring; pro-BNP — brain natriuretic peptide; VO_2 — oxygen consumption; VE/VCO_2 — minute ventilation/carbon dioxide production.

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