Begrambekova Yu. L.[1], Fedotov D. A.[1], Karanadze N. A.[1],
Lelyavina T. A.[2], Bortsova M. A.[2], Orlova Ya. A.[1]

[1] Medical Research and Educational Center, Lomonosov Moscow State University, Moscow, Russia

[2] Almazov National Medical Research Center, St. Petersburg, Russia

Possibilities of Predicting Peak Oxygen Consumption in Patients With Chronic Heart Failure According to the 6-Minute Walk Test

Aim To determine the correlation between the results of the 6-minute walk test (6MWT) and peak oxygen consumption ($VO_{2\ peak}$) for populations of patients with chronic heart failure with pronounced clinical and demographic differences; to study a possibility of indirect measurement of $VO_{2\ peak}$ based on the results of 6MWT using the formulas available from the literature.

Material and methods Two databases were analyzed: 50 patients included in the AEROFIT study (group A), and 31 patients from the Almazov National Medical Research Center (group B). The inclusion criteria were the availability of data from the cardiopulmonary stress test and the 6MWT. The possibility of predicting $VO_{2\ peak}$ was calculated based on the results of 6MWT using the formulas reported in the literature (L. P. Cahalin et al., 1996; R. M. Ross et al., 2010; R. A. Adedoyin et al., 2010). The predictive accuracy of the models was assessed using the coefficient of determination (R2). The relationship between functional and clinical-demographic indicators was assessed using the Pearson or Spearman correlation analysis.

Results The study groups differed significantly in all parameters, except for the proportion of men and the mean $VO_{2\ peak}$. Group B patients were 20 years younger than group A patients, had a lower left ventricular ejection fraction (24.06±7.75 and 41.52±10.48%, respectively; p<0.001), and covered a 130 m shorter distance in the 6MWT. Despite the absence of a significant difference in $VO_{2\ peak}$ between groups A and B (13.6 and 13.1 ml/kg/min, respectively; p=0.6581), 61% of group B patients and 20% of group A belonged to Weber functional class IV. In group A, the 6MWT distance correlated closely with $VO_{2\ peak}$ (R=0.78; p<0.01) and weakly with age (R=0.4) and body mass index (R=0.3). In group B, the 6MWT distance correlated only with $VO_{2\ peak}$ (R=0.77; p<0.01). For group A, the R. M. Ross et al. model demonstrated high accuracy in determining the mean $VO_{2\ peak}$ value with a 0.06% prediction error normalized to measured $VO_{2\ peak}$. For group B, none of the models showed satisfactory predictive accuracy. The Ross and Cahalin models showed the best coefficients of determination for groups A and B: Group A, Ross et al. (R^2=0.58) and Cahalin et al. (R^2=0.59); Group B, Ross et al. (R^2=0.59) and Cahalin et al. (R^2=0.6).

Conclusion In two groups of patients with a statistically insignificant difference in the mean values of VO_{2peak}, the mean values of 6MWT distance were significantly different, although these indicators correlated closely. The $VO_{2\ peak}$ prediction models showed satisfactory accuracy for estimation of mean VO_2, but poor accuracy for estimation of individual values. A better predictive accuracy is determined by similar clinical and demographic characteristics between the training and testing populations, and likely also by models based on larger, more diversified populations.

Keywords Chronic heart failure; cardiopulmonary stress test; peak oxygen consumption; 6-min walk test; prediction

For citations Begrambekova Yu.L., Fedotov D.A., Karanadze N.A., Lelyavina T.A., Bortsova M.A., Orlova Ya.A. Possibilities of Predicting Peak Oxygen Consumption in Patients With Chronic Heart Failure According to the 6-Minute Walk Test. Kardiologiia. 2024;64 (2):34 – 42. [Russian: Беграмбекова Ю.Л., Федотов Д.А., Каранадзе Н.А., Лелявина Т.А., Борцова М.А., Орлова Я.А. Возможности прогнозирования пикового потребления кислорода у пациентов с хронической сердечной недостаточностью по данным 6-минутного теста ходьбы. Кардиология. 2024;64 (2):34 – 42].

Corresponding author Begrambekova Yu.L. E-mail: julia.begrambekova@ossn.ru

Introduction

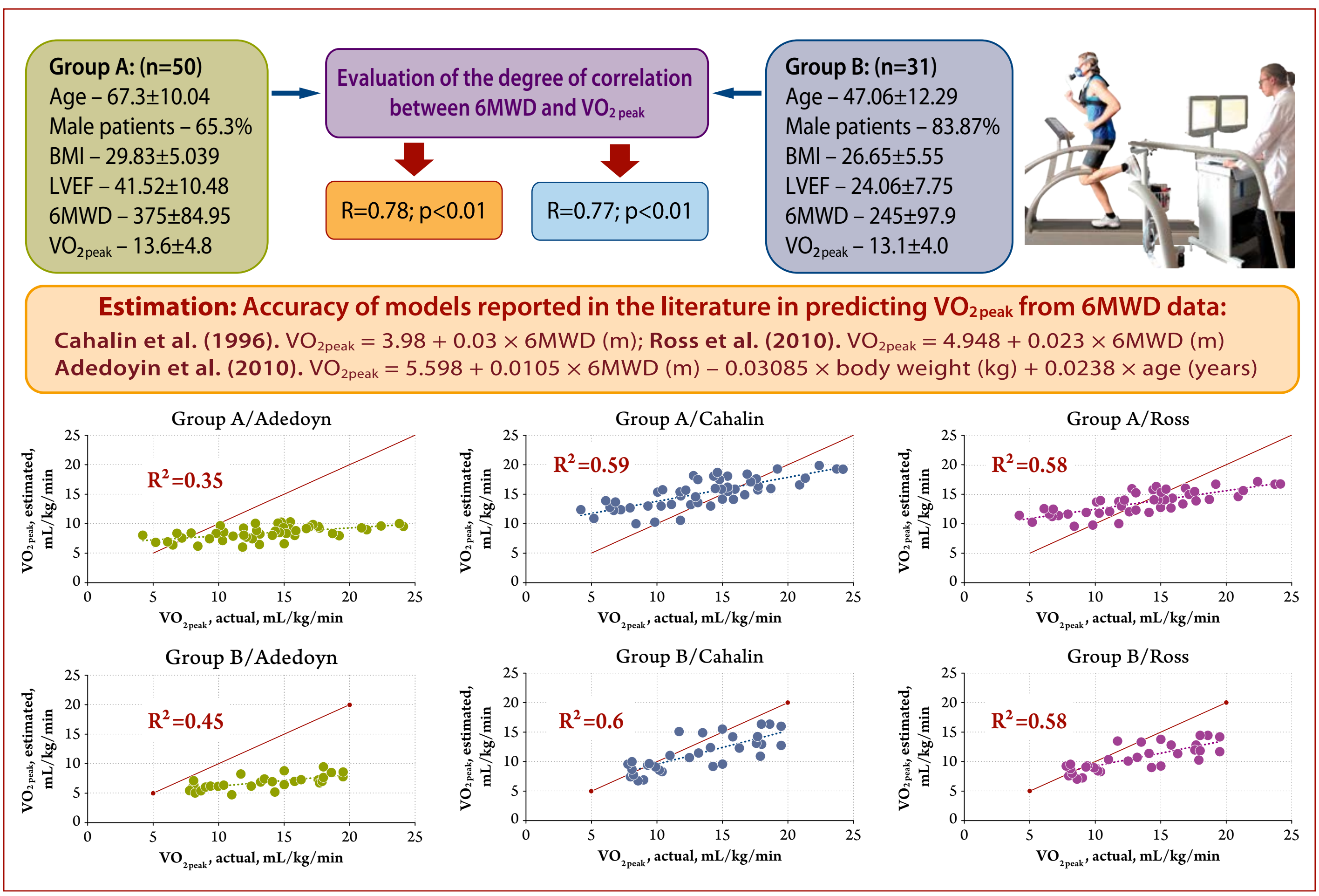
Worsening exercise tolerance is one of the most important and earliest symptoms of heart failure (HF). The severity of functional impairment is an essential adverse prognostic factor [1], determining patients' quality of life and ability to socialize [2–4]. Therefore, determining exercise tolerance has become an important clinical and research task.

In clinical practice, the two most commonly used methods to determine exercise tolerance are the 6-minute walk distance (6MWD) test and the cardiopulmonary exercise testing (CPET) [5, 6]. Despite the fact that these two tests seem to solve the same problem, they are distinguished by a fundamentally different approach to setting and fixing load levels. The ease of performing for both patient and healthcare professionals and interpreting the 6MWD test have contributed to its popularity. However, unlike CPET, the 6MWD test does not have differential diagnostic potential for load limiting factors. This test also has a strong subjective component related to a particular patient's perception of his or her comfortable pace and mental state, as it measures the distance a patient walks in 6 minutes at a comfortable pace. Thus, the 6MWD test reflects the patient's ability to tolerate normal activities of daily living.

Maximal oxygen uptake at maximal ($VO_{2\,max}$) or submaximal ($VO_{2\,peak}$) exercise, determined by CPET, is considered the gold standard for measuring the limit of cardiorespiratory endurance and has good reproducibility [7]. Peak oxygen uptake ($VO_{2\,peak}$) reflects the overall functional status of the cardiovascular, pulmonary, and skeletal-muscular systems [8], is used to identify potential candidates for heart transplantation [9–11] and provides objective data for prescribing and monitoring the effectiveness of cardiac rehabilitation [12, 13]. Peak VO_2 <14–15 (<10–13 in patients receiving beta-blockers) [14–16] is an indicator of poor prognosis in both HF patients with reduced left ventricular ejection fraction (LVEF) and patients with preserved LVEF (HFpEF). The Weber classification [17], which is still relevant and prognostically valuable, was constructed using peak oxygen uptake data (Table 1) [18]. The role of functional status assessment in determining prognosis in patients with early HF and HFpEF is particularly important. The NYHA classification has been shown to be unreliable in assessing functional impairment and poor at predicting mortality in patients with mild CHF [19]. In patients with HFpEF, the percentage of adequate $VO_{2\,peak}$ was the strongest predictor of death and heart transplantation when analyzing 5 year survival in models adjusted for age, sex, and beta-blocker therapy (Wald χ^2=15.0; hazard ratio (HR) for every 10%; P< 0.001) [20].

The prognostic value of the 6MWD test has also been repeatedly confirmed. However, some studies have reported negative results [1, 21–23]. CPET requires more time, complex and expensive equipment, and is not as easy for both patients and researchers in terms of the methodology

Central Illustration. Possibilities of Predicting Peak Oxygen Consumption in Patients With Chronic Heart Failure According to the 6-Minute Walk Test



ISSN 0022-9040. Kardiologiia. 2024;64(2). DOI: 10.18087/cardio.2024.2.n2551

Table 1. Peak oxygen uptake prediction models analyzed

Authors, paper	Formula	Study cohort
R. M. Ross et al., 2010 [29]	$VO_{2\ peak} = 4.948 + 0.023 \times 6MWD\ (m)$	Pooled data from multiple studies
R. A. Adedoyin et al., 2010 [28]	$VO_{2\ peak} = 5.598 + 0.0105 \times 6MWD\ (m) - 0.03085 \times$ body weight (kg) $+ 0.0238 \times$ age (years)	Patients with CHF class II–III
L. P. Cahalin et al., 1996 [27]	$VO_{2\ peak} = 3.98 + 0.03 \times 6MWD\ (m)$	Patients with severe CHF (class III–IV)

$VO_{2\ peak}$, peak oxygen uptake; 6MWD, 6 minute walk distance; CHF, chronic heart failure.

of the procedure and interpretation of results. As a result, the 6MWD continues to be the most widely used functional test in clinical and research practice due to its simplicity and ease of access.

Many studies have examined the relationship between 6MWD and $VO_{2\ peak}$ results. The correlation between these two indicators varied from weak to strong in different studies [21, 22, 24–26], but most studies showed a fairly strong correlation. Given this, models attempting to predict $VO_{2\ peak}$ based on 6MWD results have been proposed repeatedly. However, the high prediction accuracy of the model obtained on the training sample and described in the articles does not guarantee good performance on other samples because the degree of correlation and variance of 6MWD and $VO_{2\ peak}$ data may be different in different patient groups. Several formulas have been reported in the literature for the indirect determination of $VO_{2\ peak}$ based on the 6MWD. We selected 3 formulas [27–29] that were calculated in a population of patients with CHF and tested their prognostic accuracy in two patient populations that were as different as possible in their clinical and demographic characteristics, having previously analyzed the level of correlation between 6MWD and $VO_{2\ peak}$ data.

Objective

Determine the degree of correlation between 6MWD and $VO_{2\ peak}$ data in populations of CHF patients with significant clinical and demographic differences and explore the possibility of indirectly determining $VO_{2\ peak}$ from 6MWD using formulas available in the literature.

Material and Methods

The data for this study come from two sources. The first population is a database of patients who underwent a screening visit in the AEROFIT study (Group A, n=50). The second population is the patient database of the Almazov National Medical Research Center (Group B, n = 31). The presence of CPET and 6MWD data obtained using the same methodology were inclusion criteria for the study. Retrospective analysis of data from these patient samples was conducted.

CPET was performed using a modified Bruce protocol. During the CPET, all patients were instructed and motivated to achieve the maximum tolerated exercise load. Criteria were a respiratory efficiency of 1.10 or higher, or 16 out of 20 on the Borg scale. A 12-lead electrocardiogram was recorded throughout the CPET, and a breath-by-breath assessment was performed every 30 seconds.

Calculations were performed using formulas reported in the literature to determine if $VO_{2\ peak}$ could be predicted from the 6MWD results (Table 1).

Statistical analysis of study results

The data are presented as the means ± standard deviations or the medians and interquartile ranges depending on a type of their distribution. All quantitative indicators and parameters are presented with 95% confidence intervals (CI). The MOVER method was used to calculate CI margins for differences and percentages. The normality of data distribution was verified using the D'Agostino-Pearson criterion. Group differences were assessed using Student's t-test for normally distributed continuous variables, Mann-Whitney U-test for non-normally distributed continuous variables, and chi-squared test or Fisher's exact test for categorical variables. Univariate analysis of variance (ANOVA) or Kruskal-Wallis test was used to compare more than 2 groups. For statistically significant differences, a post hoc test with Bonferroni correction was used to detect specific group differences. Pearson or Spearman correlation analysis was used to assess the relationship between functional parameters and clinical and demographic parameters. The critical level of significance was p=0.05. In addition to statistical significance, effect sizes were estimated: coefficients of conjugacy for countable data and standardized effect size for measured data. The coefficient of determination R2 was used to assess the prediction accuracy of the models.

The AEROFIT study protocol was approved by the local ethics committee of the Medical Research and Educational Center of the Lomonosov Moscow State University (Minutes dated 16.05.2022). Coding was used to protect patient privacy. The study was conducted in accordance with international ethical conventions: the World Medical Association's Declaration of Helsinki, the International Conference on Harmonization Good Clinical Practice (ICH GCP) and the requirements of Russian legislation.

ISSN 0022-9040. Kardiologiia. 2024;64(2). DOI: 10.18087/cardio.2024.2.n2551

The routine analysis was retrospective. No additional studies were conducted. Both databases were anonymized. They contained no personal patient information and only the data needed to calculate the formulas.

Results

Table 2 provides a comparative analysis of patient clinical and demographic characteristics and functional test data.

The study groups were statistically significantly different in all parameters except percentage of male subjects and mean $VO_{2\,peak}$. Group B patients were 20 years younger, had a lower LVEF (24.06±7.75% and 41.52±10.48%, respectively), and covered a mean 6MWD of 130 m less. Furthermore, LV volumes were statistically significantly different (see Table 2). The correlation analysis showed that the $VO_{2\,peak}$ in group A was closely correlated with the 6MWD (R = 0.78). The 6MWD showed a statistically significant weak negative correlation with age (R = 0.4) and BMI (R = 0.3).

Group B showed a strong positive correlation only with the 6MWD (R=0.77; p<0.01); the 6MWD did not correlate with any other clinical and demographic parameters.

The distribution of patients by severity of CHF according to the Weber classification [17, 18] is shown in Figure 1.

As can be seen, despite the lack of a statistically significant difference in mean $VO_{2\,peak}$ between Groups A and B (13.6 mL/kg/min and 13.1 mL/kg/min, respectively; p=0.6581), 61% of patients in Group B were classified as IV, i.e. the most severe functional class according to the Weber classification, whereas there were only 20% of such patients in Group A. In both groups, patients subdivided according to the Weber classification differed statistically significantly in the 6MWD (Tabl 3). There were no statistically significant differences in any of the other indicators. Thus, for the same range of peak oxygen consumption, patients in Group A traveled a statistically significantly greater distance than patients in Group B.

The next part of the work was to determine the $VO_{2\,peak}$ for each patient in groups A and B using the formulas developed by R. M. Ross, R. A. Adedoyin and L. P. Cahalin and to analyze the prediction accuracy of these models (Table 4–9, Figure 2).

Discussion

We analyzed functional indices in two populations of CHF patients who differed significantly in terms of age and myocardial volume characteristics. Although patients in Group B were almost 20 years younger than patients in

Table 2. Comparative analysis of patient clinical and demographic characteristics and functional test data

Parameter	Group A (n = 50)	Group B (n = 31)	p
Age, mean, years	67.3 ± 10.04	47.06 ± 12.29	< 0.001
Male patients, %	65.31	83.87	0.122
BMI, kg/m²	29.83 ± 5.039	26.65 ± 5.547	0.009
LVEF, %	41.52 ± 10.48	24.06 ± 7.75	< 0.001
LVESV, mL	73.5 [49.8; 113.5]	180 [143; 264]	< 0.0001
LVEDV, mL	151.3 ± 65.5	278.3 ± 104.5	< 0.0001
$VO_{2\,peak}$, mL/kg/min	13.6 ± 4.8	13.1 ± 4.0	0.658
6MWD, m	375 ± 84.95	245 ± 97.9	< 0.001
Weber class, mean	2.86	3.45	< 0.001

The data is presented as the medians and interquartile ranges (Me [25th percentile; 75th percentile]) if not otherwise specified. BMI, body mass index; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVEDV, left ventricular end-diastolic volume; $VO_{2\,peak}$, peak oxygen uptake; 6MWD, 6 minute walk distance.

Figure 1. Distribution of patients in groups A (**A**) and B (**B**) according to the Weber classification

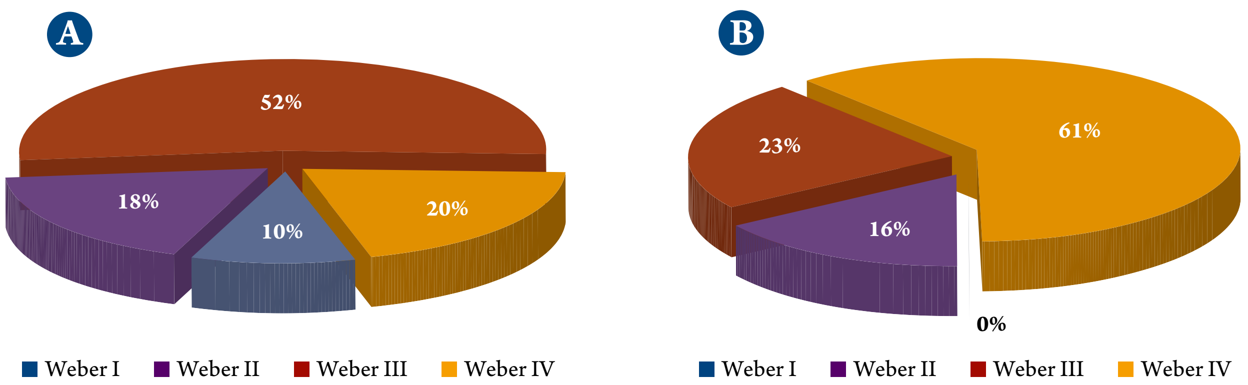


Table 3. Mean 6MWD according to CHF severity by the Weber classification, m

Weber class	Group A	Group B	p
I ($VO_{2\ peak}$ > 20 mL/kg/min)	486	—	—
II ($VO_{2\ peak}$ 16–20 mL/kg/min)	431	372	< 0.0001
III ($VO_{2\ peak}$ 10–16 mL/kg/min)	379	282.7	< 0.0001
IV ($VO_{2\ peak}$ < 10 mL/kg/min)	273.6	198.1	< 0.0001

6MWD, 6 minute walk distance; CHF, chronic heart failure.

Group A, they walked a mean of 130 m less as measured by the 6MWD test. Although the mean $VO_{2\ peak}$ values were not statistically significantly different (13.6±4.8 mL/kg/min and 13.1±4.0 mL/kg/min, respectively; p=0.658), there were more patients with more severe Weber class IV and no patients with class I in Group B. It should be noted that mean 6MWD results were statistically significantly different not only between patients in Groups A and B, but also within the same Weber class, i.e., $VO_{2\ peak}$ range. This aspect needs further discussion. The 6MWD traveled in both groups did not correlate with LVEF, end-diastolic and end-systolic volumes, which is consistent with the findings of other investigators [30]. At the same time, an important feature of the 6MWD test is that the patient chooses his or her own comfortable walking pace. In addition, if the upper limit of the distance range of a particular patient is determined by his or her level of stable aerobic metabolism, the lower limit is determined by mental characteristics and the perception of one's own physical capabilities. The known intertest variability and the presence of a learning effect when performing the 6MWD test are related to this feature of this test [31]. In fact, the CHANCE study and other studies have shown that perceived mental state, anxiety and depressive symptoms, and subjective assessment of quality of life are related to the 6MWD traveled. For example, in the CHANCE study, patients in the severe anxiety subgroup walked a shorter 6MWD (217.3±70.4 m versus 238.2±78.2 m; p=0.017). Although they also had statistically significantly higher LVEF and did not differ by CHF class. Group A patients had low mean levels of anxiety and depression on the HADS score. Unfortunately, there are no data on the mental state of Group B patients. However, it can be assumed that the level of anxiety and depression is high in young patients with severe CHF, which is supported by data from other studies [32, 33]. The correlation between the 6MWD and $VO_{2\ peak}$ data was higher in our study than in the study by Maldonado-Martín et al. (2006), which showed only a moderate correlation (r = 0.54) [34]. Among the models evaluated in our study, the model developed by Ross et al. had the highest expectations because it used

Table 4. Paired samples statistics for Group A

Measured and calculated $VO_{2\ peak}$ using the formula		Mean	n	Standard deviation	Standard error
Pair 1	$VO_{2\ peak}$, measured	13.5608	50	4.73325	0.66279
	L. P. Cahalin	15.2490	50	2.52312	0.35331
Pair 2	$VO_{2\ peak}$, measured	13.5608	50	4.73325	0.66279
	R. M. Ross	13.5686	50	1.94139	0.27185
Pair 3	$VO_{2\ peak}$, measured	13.5608	50	4.73325	0.66279
	R. A. Adedoyin	8.4196	50	1.09527	0.15337

Table 5. Pairwise sample correlations for Group A and the model's coefficient of determination

Measured and calculated $VO_{2\ peak}$ using the formula		n	Correlation	P	Coefficient of determination of the model
Pair 1	$VO_{2\ peak}$, measured/L. P. Cahalin	50	0.765	0.000	0.59
Pair 2	$VO_{2\ peak}$, measured/R. M. Ross	50	0.763	0.000	0.58
Pair 3	$VO_{2\ peak}$, measured /R. A. Adedoyin	50	0.588	0.000	0.35

Table 6. Paired samples criterion for Group A

Measured and calculated $VO_{2\ peak}$ using the formula		Paired differences						
		Prediction error	Prediction error normalized to measured VO_2, %	Standard error	95% confidence interval for the difference		Student's t-test	Significance (two-tailed)
					Lower limit	Upper limit		
Pair 1	$VO_{2\ peak}$, measured/L. P. Cahalin	-1.688	12.45	0.45388	-2.59988	-0.77659	-3.720	0.001
Pair 2	$VO_{2\ peak}$, measured/R. M. Ross	-0.008	0.06	0.48797	-0.98796	0.97228	-0.016	0.987
Pair 3	$VO_{2\ peak}$, measured /R. A. Adedoyin	5.141	37.91	0.58596	3.96424	6.31811	8.774	0.000

ISSN 0022-9040. Kardiologiia. 2024;64(2). DOI: 10.18087/cardio.2024.2.n2551

Table 7. Paired samples statistics for Group B

Measured and calculated $VO_{2\ peak}$ using the formula		Mean	N	Standard deviation	Standard error
Pair 1	$VO_{2\ peak}$	13.1032	31	3.99153	0.71690
	L. P. Cahalin	11.3368	31	2.93703	0.52751
Pair 2	$VO_{2\ peak}$	13.1032	31	3.99153	0.71690
	R. M. Ross	10.5884	31	2.25125	0.40434
Pair 3	$VO_{2\ peak}$	13.1032	31	3.99153	0.71690
	R. A. Adedoyin	6.7984	31	1.15149	0.20681

Table 8. Pairwise sample correlations for Group B and the model's coefficient of determination

Measured and calculated $VO_{2\ peak}$ using the formula		n	Correlation	P	Coefficient of determination of the model
Pair 1	$VO_{2\ peak}$, measured/L. P. Cahalin	31	0.772	> 0.001	0.60
Pair 2	$VO_{2\ peak}$, measured/R. M. Ross	31	0.771	> 0.001	0.59
Pair 3	$VO_{2\ peak}$, measured /R. A. Adedoyin	31	0.673	> 0.001	0.45

Table 9. Paired samples criterion for Group B

Measured and calculated $VO_{2\ peak}$ using the formula		Paired differences						
		Mean	Standard deviation	Standard error	95 % confidence interval for the difference		Student's t-test	Significance (two-tailed)
					Lower	Upper		
Pair 1	$VO_{2\ peak}$, measured/L. P. Cahalin	1.76645	2.54336	0.45680	0.83354	2.69936	3.867	0.001
Pair 2	$VO_{2\ peak}$, measured/R. M. Ross	2.51484	2.67207	0.47992	1.53471	3.49496	5.240	0.000
Pair 3	$VO_{2\ peak}$, measured /R. A. Adedoyin	6.30484	3.32758	0.59765	5.08427	7.52540	10.549	0.000

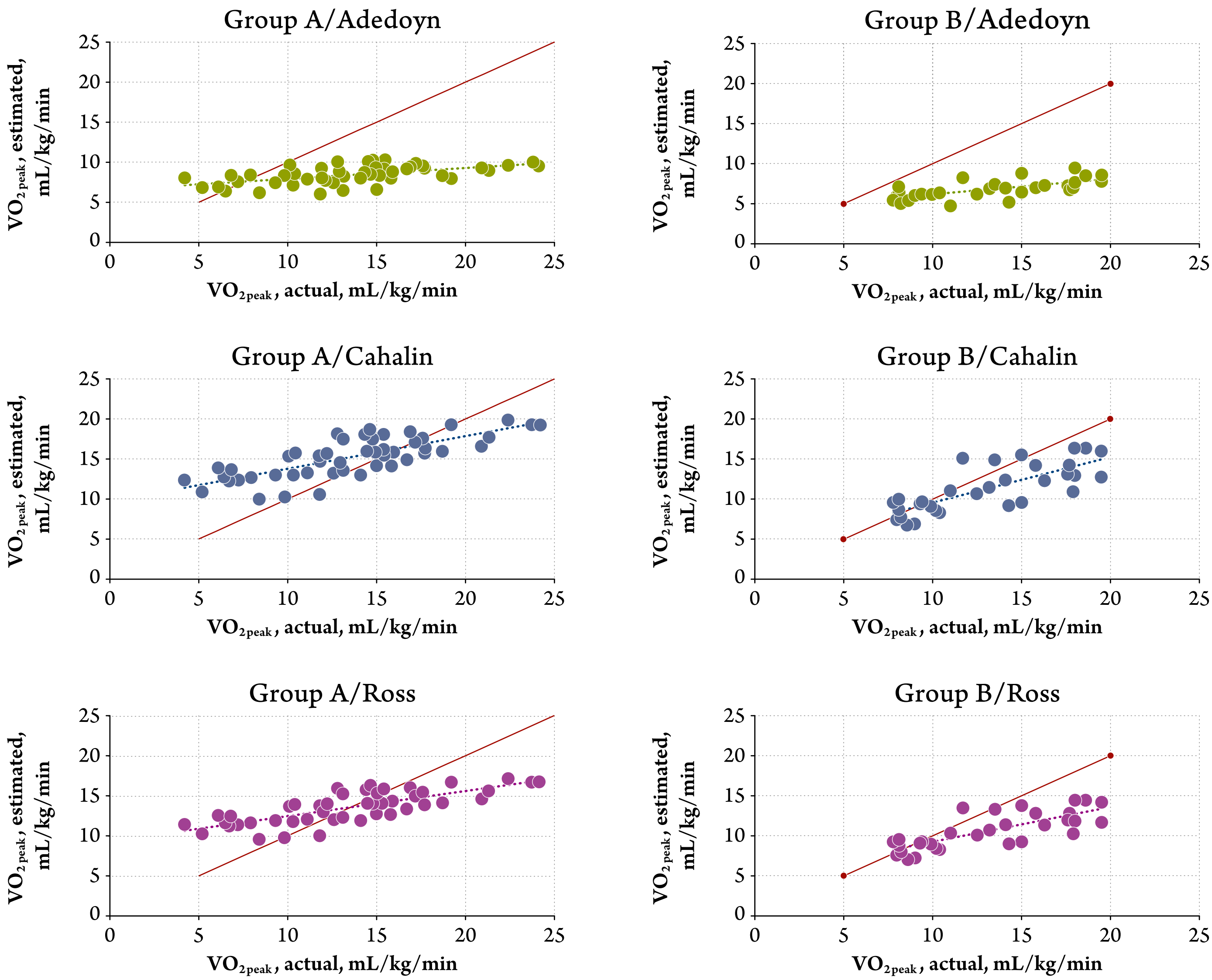
data from 1,083 patients with various cardiovascular and pulmonary diseases from 11 studies. In fact, the formula of Ross et al [29] showed a very high prediction accuracy for the mean $VO_{2\ peak}$ in Group A – the predicted mean $VO_{2\ peak}$ using this formula was almost identical to the measured mean $VO_{2\ peak}$. Completely different data were obtained in group B, where the formulas of R. M. Ross and L. P. Cahalin showed a similar low prognostic potential. The predicted mean $VO_{2\ peak}$ values were within 113–119% of the measured values, with a statistically significant difference between predicted and actual values for all formulas. Regarding the possibility of using the studied formulas to predict individual $VO_{2\ peak}$ values, we can state that these formulas did not show sufficient accuracy in our analysis, because even models with the highest coefficient of determination predicted no more than 60% of the data variability.

Thus, the results of our study showed that, despite the relatively high level of correlation between 6MWD and VO_2 data, mean 6MWD values may differ significantly in a group of patients with comparable mean $VO_{2\ peak}$. These data are further confirmation that 6MWD and CPET are not complete substitutes. The 6MWD test, in which the patient sets his or her own pace of movement, measures the patient's capacity for normal physical activity, and this capacity is determined not only by the patient's physical condition, but also by the mental components of well-being – the subjective assessment of one's health and physical abilities. Of course, this assessment can change depending on one's emotional state. Peak oxygen uptake, on the other hand, is comparable to an individual's maximum functional reserve and therefore provides a more objective assessment of an individual's status.

Developing formulas for predicting peak oxygen uptake using the 6MWD has important scientific and clinical implications and is not just a mathematical task. Possible solutions may be found on a variety of levels. For example, increasing the training sample has been used quite successfully in the Ross model – the larger the sample, the more accurate the formula. Other approaches may attempt to find new factors that explain the variance in 6MWD results. For example, making adjustments for mental state that may explain and compensate for lower than potentially possible 6MWD values for a given patient. The use of parameters that assess the degree of exertion during 6MWD, such as percent of heart rate reserve, requires further investigation.

The assessment of functional capacity is necessary to provide an objective and complete clinical portrait of the patient. For both the physician and the patient, functional status should serve not only as a marker of prognosis, but also as a starting point for the prescription

Figure 2. Scatter diagrams for calculated and measured $VO_{2\ peak}$



of rehabilitation methods and the increase of the motor activity regimen. Even a small increase in functional capacity is important for a better prognosis [23].

Limitations

Potential limitations of the study include the small number of patients in the groups and possible differences in CPET methodology due to the fact that Groups A and B were recruited at different clinical centers.

Conclusion

Despite the relatively high level of correlation, the information obtained from the 6 minute walk distance test and the cardiopulmonary exercise test are not complete substitutes for each other.

The formulas available in the literature for predicting peak oxygen uptake from 6 minute walk distance test data do not provide satisfactory accuracy for predicting individual data but can probably be used to predict mean values in clinical trials. When used in clinical trials, preference should be given to formulas that are derived from patient populations that are comparable to the study population and that have been developed on large and diverse patient populations.

Acknowledgments

The authors of the article express their gratitude to colleagues from the Federal State Budgetary Institution "National Medical Research Center named after V. A. Almazov" of the Ministry of Health of the Russian Federation for providing an anonymized database.

Funding

The study was carried out within the framework of the state assignment of the Moscow State University. M. V. Lomonosov.

No conflict of interest is reported.

The article was received on 30/08/2023

REFERENCES

1. Guazzi M, Dickstein K, Vicenzi M, Arena R. Six-Minute Walk Test and Cardiopulmonary Exercise Testing in Patients With Chronic Heart Failure: A Comparative Analysis on Clinical and Prognostic Insights. Circulation: Heart Failure. 2009;2(6):549–55. DOI: 10.1161/CIRCHEARTFAILURE.109.881326
2. Jeng C, Yang M-H, Chen P-L, Ho C-H. The Influence of Exercise Tolerance on Quality of Life Among Patients with Heart Failure. Quality of Life Research. 2004;13(5):925–32. DOI: 10.1023/B:QURE.0000025604.15624.82
3. Zhuang C, Luo X, Wang Q, Wang W, Sun R, Zhang X et al. The effect of exercise training and physiotherapy on diastolic function, exercise capacity and quality of life in patients with heart failure with preserved ejection fraction: a systematic review and meta-analysis. Kardiologia Polska. 2021;79(10):1107–15. DOI: 10.33963/KP.a2021.0101
4. Shah SJ, Cowie MR, Wachter R, Szecsödy P, Shi V, Ibram G et al. Baseline characteristics of patients in the PARALLAX trial: insights into quality of life and exercise capacity in heart failure with preserved ejection fraction. European Journal of Heart Failure. 2021;23(9):1541–51. DOI: 10.1002/ejhf.2277
5. Guyatt GH, Sullivan MJ, Thompson PJ, Fallen EL, Pugsley SO, Taylor DW et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. Canadian Medical Association Journal. 1985;132(8):919–23. PMID: 3978515
6. Ingle L, Witte KK, Cleland JGJF, Clark AL. The prognostic value of cardiopulmonary exercise testing with a peak respiratory exchange ratio of <1.0 in patients with chronic heart failure. International Journal of Cardiology. 2008;127(1):88–92. DOI: 10.1016/j.ijcard.2007.04.075
7. Marburger CT, Brubaker PH, Pollock WE, Morgan TM, Kitzman DW. Reproducibility of cardiopulmonary exercise testing in elderly patients with congestive heart failure. The American Journal of Cardiology. 1998;82(7):905–9. DOI: 10.1016/s0002-9149(98)00502-5
8. Cahalin LP, Chase P, Arena R, Myers J, Bensimhon D, Peberdy MA et al. A meta-analysis of the prognostic significance of cardiopulmonary exercise testing in patients with heart failure. Heart Failure Reviews. 2013;18(1):79–94. DOI: 10.1007/s10741-012-9332-0
9. Riebe D, Ehrman JK, Liguori G, Magal M. ACSM's guidelines for exercise testing and prescription. - Philadelphia: Wolters Kluwer; 2018. – 472p. ISBN 978-1-4963-3906-5
10. ATS/ACCP Statement on Cardiopulmonary Exercise Testing. American Journal of Respiratory and Critical Care Medicine. 2003;167(2):211–77. DOI: 10.1164/rccm.167.2.211
11. Tereshchenko S.N., Galyavich A.S., Uskach T.M., Ageev F.T., Arutyunov G.P., Begrambekova Yu.L. et al. 2020 Clinical practice guidelines for Chronic heart failure. Russian Journal of Cardiology. 2020;25(11):311–74. [Russian: Терещенко С.Н. Галявич А.С., Ускач Т.М., Агеев Ф.Т., Арутюнов Г.П., Беграмбекова Ю.Л. et al. Хроническая сердечная недостаточность. Клинические рекомендации 2020. Российский кардиологический журнал. 2020;25(11):311-74]. DOI: 10.15829/1560-4071-2020-4083
12. Galenko VL, Lelyavina TA, Sitnikova MY. Response predictors for physical training HFrEF patients. Kardiologiia. 2018;58(S4):22–8. [Russian: Галенко В.Л., Лелявина Т.А., Ситникова М.Ю. Предикторы недостаточного ответа на физические тренировки у больных ХСН. Кардиология. 2018;58(S4):22-8]. DOI: 10.18087/cardio.2434
13. Swank AM, Horton J, Fleg JL, Fonarow GC, Keteyian S, Goldberg L et al. Modest Increase in Peak VO_2 Is Related to Better Clinical Outcomes in Chronic Heart Failure Patients: Results From Heart Failure and a Controlled Trial to Investigate Outcomes of Exercise Training. Circulation: Heart Failure. 2012;5(5):579–85. DOI: 10.1161/CIRCHEARTFAILURE.111.965186
14. Lala A, Shah KB, Lanfear DE, Thibodeau JT, Palardy M, Ambardekar AV et al. Predictive Value of Cardiopulmonary Exercise Testing Parameters in Ambulatory Advanced Heart Failure. JACC: Heart Failure. 2021;9(3):226–36. DOI: 10.1016/j.jchf.2020.11.008
15. Corrà U, Giordano A, Piepoli M. Cardiopulmonary exercise testing in chronic heart failure patients treated with beta-blockers: Still a valid prognostic tool. International Journal of Cardiology. 2020;317:128–32. DOI: 10.1016/j.ijcard.2020.04.020
16. Guimaraes GV, d'Avila VM, Silva MS, Ferreira SA, Ciolac EG, Carvalho VO et al. A cutoff point for peak oxygen consumption in the prognosis of heart failure patients with beta-blocker therapy. International Journal of Cardiology. 2010;145(1):75–7. DOI: 10.1016/j.ijcard.2009.05.001
17. Weber KT, Kinasewitz GT, Janicki JS, Fishman AP. Oxygen utilization and ventilation during exercise in patients with chronic cardiac failure. Circulation. 1982;65(6):1213–23. DOI: 10.1161/01.CIR.65.6.1213
18. Guazzi M, Borlaug B, Metra M, Losito M, Bandera F, Alfonzetti E et al. Revisiting and Implementing the Weber and Ventilatory Functional Classifications in Heart Failure by Cardiopulmonary Imaging Phenotyping. Journal of the American Heart Association. 2021;10(5):e018822. DOI: 10.1161/JAHA.120.018822
19. Zimerman A, Da Silveira AD, Borges MS, Engster PHB, Schaan TU, De Souza GC et al. Functional assessment based on cardiopulmonary exercise testing in mild heart failure: A multicentre study. ESC Heart Failure. 2023;10(3):1689–97. DOI: 10.1002/ehf2.14287
20. Shafiq A, Brawner CA, Aldred HA, Lewis B, Williams CT, Tita C et al. Prognostic value of cardiopulmonary exercise testing in heart failure with preserved ejection fraction. The Henry Ford HospITal CardioPulmonary EXercise Testing (FIT-CPX) project. American Heart Journal. 2016;174:167–72. DOI: 10.1016/j.ahj.2015.12.020
21. Lucas C, Stevenson LW, Johnson W, Hartley H, Hamilton MA, Walden J et al. The 6-min walk and peak oxygen consumption in advanced heart failure: aerobic capacity and survival. American Heart Journal. 1999;138(4 Pt 1):618–24. DOI: 10.1016/s0002-8703(99)70174-2
22. Opasich C. Six-minute walking performance in patients with moderate-to-severe heart failure; is it a useful indicator in clinical practice? European Heart Journal. 2001;22(6):488–96. DOI: 10.1053/euhj.2000.2310
23. Fuentes-Abolafio IJ, Stubbs B, Pérez-Belmonte LM, Bernal-López MR, Gómez-Huelgas R, Cuesta-Vargas AI. Physical functional performance and prognosis in patients with heart failure: a systematic review and meta-analysis. BMC Cardiovascular Disorders. 2020;20(1):512. DOI: 10.1186/s12872-020-01725-5
24. Rostagno C, Galanti G, Romano M, Chiostri G, Gensini GF. Prognostic value of 6-minute walk corridor testing in women with mild to moderate heart failure. Italian Heart Journal: Official Journal of the Italian Federation of Cardiology. 2002;3(2):109–13. PMID: 11926008
25. Šagát P, Kalčik Z, Bartik P, Šiška Ľ, Štefan L. A Simple Equation to Estimate Maximal Oxygen Uptake in Older Adults Using the 6 min Walk Test, Sex, Age and Body Mass Index. Journal of Clinical Medicine. 2023;12(13):4476. DOI: 10.3390/jcm12134476
26. Zotter-Tufaro C, Mascherbauer J, Duca F, Koell B, Aschauer S, Kammerlander AA et al. Prognostic Significance and Determinants of the 6-Min Walk Test in Patients With Heart Failure and Preserved Ejection Fraction. JACC: Heart Failure. 2015;3(6):459–66. DOI: 10.1016/j.jchf.2015.01.010
27. Cahalin LP, Mathier MA, Semigran MJ, Dec GW, DiSalvo TG. The Six-Minute Walk Test Predicts Peak Oxygen Uptake and Survival in Patients With Advanced Heart Failure. Chest. 1996;110(2):325–32. DOI: 10.1378/chest.110.2.325
28. Adedoyin RA, Adeyanju SA, Balogun MO, Adebayo RA, Akintomide AO, Akinwusi PO. Prediction of functional capacity during six-minute walk among patients with chronic heart failure. Nigerian Journal of Clinical Practice. 2010;13(4):379–81. PMID: 21220849
29. Ross RM, Murthy JN, Wollak ID, Jackson AS. The six minute walk test accurately estimates mean peak oxygen uptake. BMC Pulmonary Medicine. 2010;10(1):31. DOI: 10.1186/1471-2466-10-31
30. Higginbotham MB, Morris KG, Conn EH, Coleman RE, Cobb FR. Determinants of variable exercise performance among patients with

severe left ventricular dysfunction. The American Journal of Cardiology. 1983;51(1):52–60. DOI: 10.1016/S0002-9149(83)80010-1

31. Wu G, Sanderson B, Bittner V. The 6-minute walk test: How important is the learning effect? American Heart Journal. 2003;146(1):129–33. DOI: 10.1016/S0002-8703(03)00119-4
32. Vermeulen KM, Bosma OH, Bij WVD, Koeter GH, TenVergert EM. Stress, psychological distress, and coping in patients on the waiting list for lung transplantation: an exploratory study. Transplant International. 2005;18(8):954–9. DOI: 10.1111/j.1432-2277.2005.00169.x
33. Porter RR, Krout L, Parks V, Gibbs S, Luers ES, Nolan MT et al. Perceived stress and coping strategies among candidates for heart transplantation during the organ waiting period. The Journal of Heart and Lung Transplantation. 1994;13(1 Pt 1):102–7. PMID: 8167114
34. Maldonado-Martin S, Brubaker PH, Kaminsky LA, Moore JB, Stewart KP, Kitzman DW. The Relationship of a 6-min Walk to $VO_{2\ peak}$ and VT in Older Heart Failure Patients. Medicine & Science in Sports & Exercise. 2006;38(6):1047–53. DOI: 10.1249/01.mss.0000222830.41735.14

ISSN 0022-9040. Kardiologiia. 2024;64(2). DOI: 10.18087/cardio.2024.2.n2551