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Selection of the optimal respiratory muscle training mode in patients with class II-III chronic heart failure

Aim To study the effect of various types of respiratory muscle training (RMT) in patients with functional class (FC) II-III chronic heart failure (CHF) and more than 70% preserved diaphragm muscle mass.

Material and methods 53 patients (28 men and 25 women) aged 50-75 years with NYHA FC II-III ischemic heart disease (IHD) and arterial hypertension with more than 70% preserved diaphragm muscle mass of >70% were randomized to one of four RMT types: static loads, dynamic loads, their combination, and breathing without applied resistance as a control. Peak oxygen consumption ($VO_{2\ peak}$) and maximum inspiratory pressure (MIP) were evaluated at baseline and in 6 months.

Results All study groups showed significant improvement of physical endurance indexes compared to baseline values ($p<0.05$). In pairwise comparison, the groups significantly differed ($p<0.01$). The greatest improvement was observed for patients of dynamic and combined training groups. Furthermore, in the combined training group, results were significantly higher than in the group of isolated dynamic loads. The most significant ($p<0.01$), positive changes in the force of inspiratory muscles were observed in groups of dynamic and combined trainings with the best results displayed by patients of the combined training group.

Conclusion With preserving more than 70% of diaphragm muscle tissue (as determined by MIP >60 cm H_2O), a combination of static and dynamic RMT is most effective for patients with FC II-III CHF.

Keywords Chronic heart failure; CHF FC; diaphragm; maximum inspiratory pressure; respiratory muscle training

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Introduction

Respiratory muscle training in patients with chronic heart failure (CHF) has proven effective and is included in the national and European guidelines for the physical rehabilitation of CHF patients [1–5].

Souza et al. [6] showed in their prospective study that respiratory muscle training increases maximal diaphragm thickness during contraction and improves pulmonary function.

In our recent study [7], the analysis of diaphragm autopsy and life-time functional tests showed that there is a close and direct correlation between peak inspiratory pressure (PIP). This implicitly shows the functional state of respiratory muscles, including diaphragm muscle [8,10], and muscle tissues, and an indirect correlation with adipose and connective tissues in the diaphragm. During the study, we found that 70% of the preserved diaphragm muscle mass corresponded to PIP equal to 60 cmH_2O. The most significant decrease in PIP is observed in patients with CHF functional class (FC) III, and PIP remains low in patients with CHF FC IV [7].

In other words, the more muscle tissue is preserved in the diaphragm, the more it will contribute to efficient external respiration and the possibility of increasing inspiratory volume in proportion to increased physical activity.

The objective of this study was to examine the effects of various respiratory muscle training in patients with CHF FC II–III and more than 70% preserved diaphragm muscle mass (PIP more than 60 cmH_2O).

Material and methods

The study was carried out in City Clinical Hospital No. 4 in Moscow and approved by the ethics committee of the Pirogov Russian National Research Medical University.

Inclusion criteria: Patients with CHF FC II–III in a stable condition, more than 70% preserved diaphragm muscle mass (PIP > 60 cmH_2O), 50–75 years old, signed informed consent. CHF was diagnosed by blood levels of NT-proBNP (not less than 125 pg/mL) [11].

Exclusion criteria: Clinically significant comorbidity, severe renal and/or hepatic failure, acute infectious disease, severe chronic obstructive pulmonary disease, emphysema, cancer, anemia, valvular diseases, diaphragm muscle pathology, frequent recurrent clinically significant hydrothorax, pneumothorax, obstructive atelectasis, pulmonary tuberculosis, interstitial pulmonary diseases, tense ascites, alcohol abuse, substance abuse, smoking, and psychological disorders. Patients with unstable angina, patients in the early post-infarction period, patients receiving prolonged mechanical ventilation, and patients with a body mass index (BMI) less than 20 kg/m^2 or more than 32 kg/m^2 were excluded from the study.

Clinical characteristics of patients

The study included 53 patients (28 males and 25 females) aged 50 to 75, with CHD and/or hypertensive heart disease and CHF FC II–III. CHF FC II was diagnosed in 31 patients, FC III in 22 patients. The median duration of CHF was 2 years (the interquartile range was 2). The median BMI was 25 kg/m^2 (interquartile range was 2). 15 patients had permanent atrial fibrillation, 7 patients had a pacemaker implanted. Twenty-six patients had a history of myocardial infarction, and eight patients underwent coronary artery bypass grafting.

Standard CHF therapy was administered: angiotensin-converting enzyme inhibitors above the half-maximal dose (n=52), beta-blockers above the half-maximal dose (n=53), mineralocorticoid receptor antagonists (n=31), diuretics (n=23), digoxin (n=5), warfarin (n=5), new oral anticoagulants (n=10), acetylsalicylic acid (n=22), hypolipidemic therapy (n=53), adequate hypotensive therapy.

Patients were randomized by means of random numbers to one of four respiratory muscle training options: static exercises, dynamic exercises, a combination of static and dynamic exercises, and the control group of unresisted breathing.

Baseline peak oxygen consumption (VO_{2peak}) and PIP were not significantly different in these four groups (Table 1).

Baseline comparative indicators of subjects are provided in Table 1.

Table 1. Baseline patient characteristics

Parameter		Control group	Static exercises	Dynamic exercises	Mixed exercises	Significance of differences between groups*
Number of observations		11	14	14	14	–
Female, %		36.4	42.9	50.0	57.1	0.747
Age, years	Mean	64.1	66.3	66.4	68.0	0.819
	Median	67.0	67.5	67.0	68.0	
	Minimum	50.0	54.0	58.0	55.0	
	Maximum	75.0	75.0	75.0	75.0	
	Standard deviation	10.7	7.3	4.9	5.6	
Patients with FC III, %		36	29	43	57	0.474
PIP, cmH_2O	Mean	66.1	68.4	67.2	66.9	0.683
	Median	65.0	70.0	66.0	67.5	
	Minimum	60.0	60.0	60.0	60.0	
	Maximum	73.0	74.0	74.0	72.0	
	Standard deviation	4.9	4.6	4.6	4.7	
VO_{2peak}, mL/kg/min	Mean	12.0	12.8	12.2	12.5	0.454
	Median	11.6	13.1	11.7	12.7	
	Minimum	10.2	10.5	10.5	10.4	
	Maximum	14.7	14.6	14.3	14.2	
	Standard deviation	1.5	1.4	1.5	1.4	

* – the quantitative variables (inspiration force, oxygen consumption, age) were compared using the Kruskal–Wallis test, and nominal variables (sex, NYHA class) were compared using the χ^2 test. PIP, peak inspiratory pressure; VO_{2peak}, peak oxygen consumption.

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The follow-up period was six months. The implementation of training was controlled by monthly telephone calls.

All patients underwent the following examinations at baseline and after six months: echocardiography with left ventricular ejection fraction (LVEF) calculation using the Simpson method, ECG Holter monitoring to rule out malignant arrhythmias, spirometry.

The respiratory muscle force was measured by PIP using an electronic sensor (micro RPM, Cardinal Health).

$VO_{2\ peak}$ and other parameters of physical tolerance were assessed using a cardiopulmonary test on a CARDIOVIT CS-200 Ergo-Spiro ergospyrometry system following the guidelines of the American Thoracic Society for the modified Bruce protocol with stagewise loading [12] at baseline and after six months of training. The test ended when symptoms of fatigue and/or dyspnea assessed ≥17 on the Borg scale (very severe) appeared. [13]

Respiratory muscles were trained using a Threshold IMT® Breathing trainer, providing additional inspiratory resistance [14, 16]. Training was conducted following our original techniques [5].

Dynamic load protocol

The patient places a nose clip on his/her nose, then places the trainer mouth piece in his/her mouth and seals it with his/her lips, then breathes in for 2–4 seconds and out for 4–6 seconds. After 1–2 minutes of calm breathing, this maneuver is repeated to prevent hyperventilation.

The initial resistance of the trainer is set at 9 cmH_2O. Every third to fifth training session, the load intensity is increased by 2 cmH_2O depending on the patient's condition. The duration of a training session is 15–20 minutes. The frequency is 3–5 training sessions per week.

Static load protocol

Стартовое сопротивление воздушной струе тренажера устанавливается на уровне 9 см вод. ст., после чего пациент, плотно обхватив тренажер губами, делает вдох, удерживая сопротивление на тренажере в течение 3–5 сек. Далее пациент спокойно дышит в течение 1–3 мин. Продолжительность тренировки – 15–20 мин. Частота тренировок – 3–5 в неделю.

Combined load protocol

The patient alternates static and dynamic loads: 1 dynamic load cycle, 1–2 min rest to prevent hyperventilation, 1 static load cycle, 1–2 min rest with subsequent repetition of a sequence of loads. The duration of a training session is 15–20 minutes. The frequency is 3–5 training sessions per week. The training results were assessed six months later.

Table 2. Comparison of patient groups based on the results of different respiratory muscle training modes after six months

Parameter		Control group	Static exercises	Dynamic exercises	Mixed exercises	Significance of intergroup differences*
ΔMIP cmH_2O	Mean	1,5	5,3	12,9	23,6	0,000
	Median	2,0	5,0	13,0	23,5	
	Minimum	0,0	2,0	9,0	13,0	
	Maximum	2,0	12,0	19,0	36,0	
	Standard deviation	0,7	2,7	2,4	6,2	
$\Delta VO_{2\,peak}$, mL/kg/min	Mean	0,2	0,9	1,8	3,5	0,000
	Median	0,2	0,8	1,8	3,4	
	Minimum	0,0	0,5	1,4	2,1	
	Maximum	0,4	1,4	2,4	4,9	
	Standard deviation	0,1	0,3	0,3	0,8	

Statistical analysis

The data obtained in the study was processed using the IBM SPSS Statistics 25 software suite. Numeric variables were analyzed using only non-parametric tests: indicators of respiratory activity (inspirational force, level of oxygen consumption), and other individual variables (age) were not normally distributed (graphical analysis and Shapiro – Wilk goodness-of-fit test).

The data analysis was carried out in 2 stages:
(a) verification of the comparability of patient groups,
(b) assessment of the relationship between training and changes in respiratory activity.

In both cases, inter-group differences were tested using the Kruskal – Wallis test for the numeric variables (age, indicators of respiratory activity) and the χ^2 test for the categorical variables (sec, NYHA classes). All comparisons were performed on the significance level of p=0.05. The groups were compared using post-hoc pairwise comparisons with the Mann–Whitney test and Bonferroni adjustment.

Results

Of a total of 53 patients included, 49 patients completed the study. Four patients (two from the static group and one from the dynamic group, and one from the combination group) were withdrawn due to poor compliance to training (less than 40%). No deaths occurred in the study groups during the follow-up period. During the study, changes in CHF management were made only in the control group: three patients required an increase of diuretic therapy due to decompensation of heart failure.

In the combined group, three patients were hospitalized due to an attack of atrial fibrillation. In the static group, five patients were hospitalized for the same reason. In the dynamic group, five patients were hospitalized for abnormal heart rhythm. Three patients in the control group were hospitalized for decompensation of blood circulation. Two subjects of the control group suffered pneumonia.

Six months after the initiation of the study, the functional tolerance in terms of $VO_{2\,peak}$ increased in all patient groups (Figure 1, Table 2).

The improvement in physical tolerance was observed in all study groups and was statistically significant versus the baseline values ($p<0.05$). The pairwise comparisons (Table 1) showed significant differences between the groups ($p<0.01$). The best improvements were observed in the patients of the groups of dynamic and combined exercises. Notably, the results in the combined exercise group were significantly higher than in the dynamic exercise group.

Respiratory muscle strength increased in all the exercise groups (Figure 1, Table 2).

There were significant intergroup differences in the increase of both inspiration force and oxygen consumption. Moreover, all pairwise differences were significant at p=0.0085 (the minimum level necessary to confirm the differences in six intergroup comparisons). It can be reliably argued that the improvements in the group of static-dynamic training were the highest. In the group with dynamic training, it was higher than in the groups with static training and the control group. In the group with static training, it was higher than in the control group.

Thus, the most significant positive changes in inspiratory muscle force were observed in the groups of dynamic and combination training, with the best results being achieved in the latter.

Thus, combination training was the most effective in improving the condition of respiratory muscles by PIP. Maximum improvement in the functional condition in terms of VO_{2peak} was observed in this group. Thus, the most

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effective training for patients with CHF with the most preserved diaphragm muscle mass is the combination of static and dynamic breathing exercises.

Discussion

Several recent studies have shown that respiratory muscle training contributes to the efficacy of rehabilitation in CHF patients [17–23]. Respiratory muscle training increases strength and tolerance of the respiratory muscles [1,2,24–27] and efficacy of gas exchange, thus improving spirometry performance and oxygen saturation of arterial blood, which contributes to partial regression of metabolic disorders in respiratory muscles [1, 28–31]. This in turn reduces dyspnea and increases tolerance to physical load [1, 2, 25–27, 32–37].

The initial condition of the diaphragm muscle and the degree of its morphological remodeling is a factor limiting the potential efficacy of respiratory muscle training in CHF patients. Morphological tests in the recent study showed that, as CFH progresses, the muscle tissue is substituted by adipose and connective tissues. This process begins in the diaphragm earlier than in the peripheral muscles [7]. Since substitution of muscle tissue by connective tissue is of individual nature, these changes can be used to develop personalized training programs. We wanted to find out how effective the different modes of respiratory muscle training can be in patients with preserved diaphragm muscle mass.

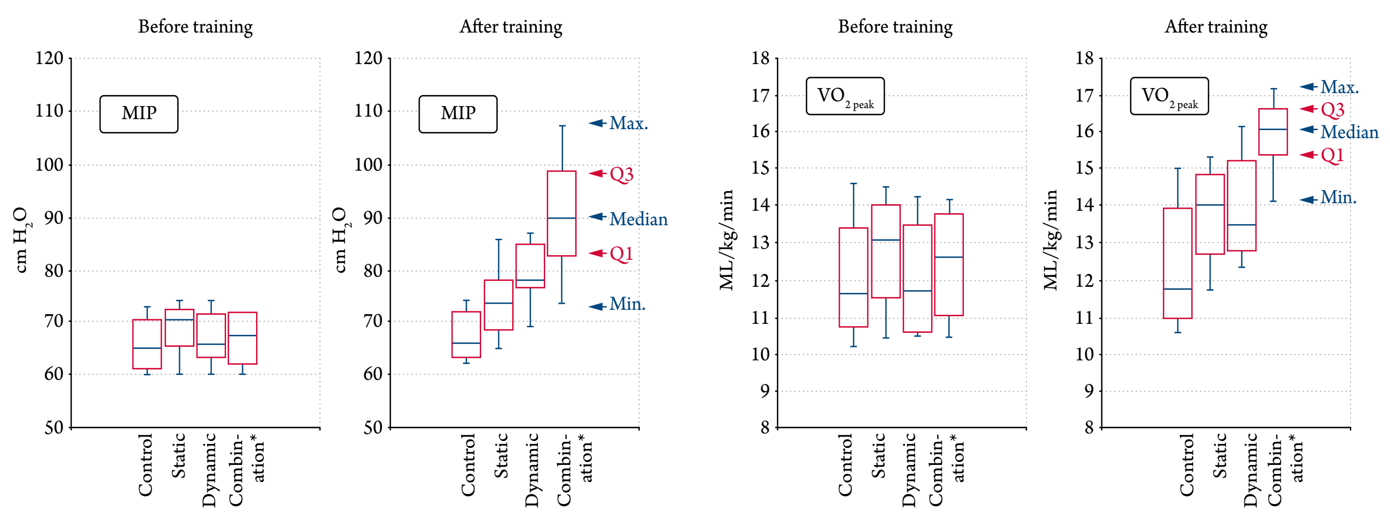
The exact mechanisms by which the resistance exercises influence morphological changes in the diaphragm muscle are not well-known. However, a prospective study [6] showed that such training promoted an increase in the maximum thickness of the diaphragm muscle. The most likely mechanism of such changes may be the developing hypertrophy of the remaining functioning muscle fibers, which helps to increase the inspiration force.

This study included patients with CHF and diaphragm muscle mass >70% of the total diaphragm mass, which allowed effective hypertrophy of the diaphragm muscle fibers to be achieved and inspiration force in these patients during training to be increased. Analysis of changes in the inspiration force in different training modes showed that combination training contributes to the greatest increase in inspiration force. The mean increase in PIP in this group was 23.6 cmH_2O.

Analysis of the efficacy of static exercises is of particular interest. We did not find large studies of the effects of static exercises on the long-term prognosis in patients with CHF. In our study, the comparison of these patients with patients who performed dynamic exercises and achieved a mean increase in PIP of 12.9 cmH2O, showed less efficacy of static exercises. The mean PIP gain in this group was minimal – 5.3 cmH_2O. Thus, static exercises in CHF patients with preserved diaphragm muscle mass are less effective than dynamic exercises. However, a combination of static and dynamic exercises promoted significant increases in PIP, which is an integral indicator of changes of the diaphragm muscle mass, mainly in comparison with other types of exercise. It is unclear why the combination of exercises lead to such significant changes in PIP, and why static exercises alone were not so effective.

The mechanics of favorable influence of combined dynamic and static exercises on preserved diaphragm muscle tissue is unclear and requires further clarification. However, we can assume a higher efficacy of the combination of dynamic and static exercises, in order to train the respiratory muscles in CHF patients with preserved diaphragm muscle mass.

Figure 1. Quartile distribution of peak inspiratory pressure and peak oxygen consumption before and after training



$VO_{2\,peak}$, peak oxygen consumption. PIP, peak inspiratory pressure. Control, control group; static, static exercises, dynamic, dynamic exercises, combination, the combination of static and dynamic exercises.

Limitations

The analysis did not include patients excluded due to poor compliance with the recommended exercises. The index used which indicates preservation of more than 70% of diaphragm muscle mass in patients with CHN (PIP 60 cmH_2O) was based on the previously established high correlation between PIP and the percentage of muscle mass in the diaphragm. It is not possible to carry out a sufficiently broad study to evaluate the sensitivity and specificity of this criterion and obtain reliable results due to the limited window between life-time functional tests and subsequent post-mortem examination. This study continues, but we have managed to include seven patients in the study in the past year.

Conclusion

A comparison of the three modes of respiratory muscle training (dynamic, static, and combination) allows it to be assumed that the combination of dynamic and static exercises is the most promising method of long-term training of respiratory muscles in patients with CHF FC II–III and the preservation of more than 70% of the diaphragm muscle tissue (PIP>60 cm H_2O).

No conflict of interest is reported.

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