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# ТРЕНИРОВКА ДЫХАТЕЛЬНОЙ МУСКУЛАТУРЫ В КОМПЛЕКСНОМ ЛЕЧЕНИИ ПАЦИЕНТОВ С ОСТРОЙ ДЕКОМПЕНСАЦИЕЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ

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# Respiratory Muscles Training in the Complex Treatment of Patients with Acute Decompensated Heart Failure

#### Резюме

Цель: оценить эффективность тренировки дыхательной мускулатуры в комплексном лечении пациентов с острой декомпенсацией сердечной недостаточности. Материал и методы. В проспективное рандомизированное исследование были включены 120 пациентов (71 мужчина и 49 женщин, средний возраст 73,6±5,8лет), госпитализированных с острой декомпенсацией сердечной недостаточности. Основными критериями исключения были: необходимость лечения в условиях отделения интенсивной терапии; гемодинамическая нестабильность; тяжелая бронхопульмональная и другая сопутствующая патология. После прохождения процедур исходного обследования все пациенты были рандомизированы в группу дыхательной гимнастики, выполняемой в дополнение к стандартной медикаментозной терапии (основная группа, п=60) либо в группу только стандартной медикаментозной терапии (контрольная группа, п=60). Пациенты основной группы были обучены технике полного йоговского дыхания, состоящего из трех последовательных фаз: брюшного, грудного и ключичного. Участники практиковали полное дыхание ежедневно не менее 3 раз в день по 10 минут под наблюдением инструктора. Первичной конечной точкой исследования было изменение выраженности одышки согласно модифицированной шкале Борга (в модификации Мареева В.Ю.) на 7-й день лечения. Результаты. На фоне лечения у пациентов обеих групп значимо уменьшилась выраженность одышки, в большей степени в группе дыхательной гимнастики (с 6 (5; 6) до 3 (2; 3)) баллов) по сравнению с контрольной (с 6 (5; 6) до 4 (3; 4), р <0,05). Значимые различия между группами были получены и по вторичным переменным эффективности: дистанции теста с шестиминутной ходьбой, частоте сердечных сокращений и дыхания в покое, насыщению крови кислородом (р < 0,05). У пациентов, выполнявших дыхательную гимнастику, масса тела снижалась быстрее (0,72±0,06 кг/сут против 0,53±0,06 кг/сут, p <0,001), хотя объемы выделенной жидкости между группами не различались. В среднем в основной группе влажные хрипы в легких были купированы к шестому дню от момента госпитализации (интерквартильный интервал 5-7 дней), а в контрольной — к восьмому (интерквартильный интервал 7-9 дней), р=0,024. Продолжительность активной фазы диуретической терапии и среднесуточные дозы диуретиков были ниже в основной группе по сравнению с контрольной (р <0,05). За вре-

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мя госпитализации в обеих группах больных наблюдалось заметное улучшение качества жизни, однако степень его была более выражена у пациентов, практикующих полное дыхание (р <0,01). Госпитальная летальность и частота переводов в отделение интенсивной терапии не различались между группами. Средние сроки госпитализации у выживших пациентов оказались значимо меньше в основной группе, чем в контрольной (14,2±2,5 против 17,3±2,9, р <0,001). Заключение. Тренировка дыхательной мускулатуры с помощью полного йоговского дыхания в дополнение к стандартной медикаментозной терапии пациентов с острой декомпенсацией сердечной недостаточности приводит к более значимому уменьшению выраженности одышки, увеличению толерантности к физической нагрузке, улучшению насыщения крови кислородом и снижению потребности в диуретиках. Применение полного дыхания ассоциируется с заметным улучшением качества жизни пациентов, более быстрым достижением компенсации и уменьшением сроков пребывания в стационаре, однако не приводит к улучшению госпитальных исходов заболевания.

**Ключевые слова:** хроническая сердечная недостаточность, декомпенсация, полное йоговское дыхание, одышка, качество жизни, диуретики, сроки госпитализации, летальность

## Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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#### **Abstract**

The aim: to evaluate the efficacy of respiratory muscles training in the complex treatment of patients with acute decompensated heart failure. Material and methods. A prospective randomized study included 120 patients (71 men and 49 women, mean age 73,6±5,8 years) hospitalized with acute decompensated heart failure. The main exclusion criteria were: requirement for treatment in intensive care unit; hemodynamic instability; severe pulmonary and other concomitant pathology. After initial procedures all patients were randomized to breathing exercises performed in addition to standard therapy (main group, n=60) or to standard therapy only (control group, n=60). Patients of the main group were trained in the technique of complete yogic breathing, which consists of three successive phases: abdominal, thoracic and clavicular. The participants practiced full breathing daily at least 3 times a day for 10 minutes under the supervision of instructor. The primary endpoint of the study was the change in dyspnea according to the modified Borg scale (modified by V.Yu. Mareev) on the 7th day of treatment. Results. During treatment the severity of dyspnea decreased in both groups, more significantly in the main group (from 6 (5; 6) to 3 (2; 3) points) compared to control (from 6 (5; 6) to 4 (3; 4) points, p <0,05). Significant differences between the groups were also obtained for the secondary variables of efficacy: six-minute walk distance, heart rate and breathing rate at rest, blood oxygen saturation (p <0,05). In patients who performed breathing exercises, body weight decreased faster (0,72±0,06 kg/day versus 0,53±0,06 kg/day, p <0,001), although the volumes of excreted fluid did not differ between the groups. In the main group moist rales in the lungs were stopped by the sixth day of hospitalization (interquartile range of 5-7 days), and in the control group — by the eighth (interquartile range of 7-9 days), p=0,024. The duration of active diuretic phase and the average daily doses of diuretics were lower in main group compared to control (p <0,05). During hospitalization quality of life improved in both groups, more significantly in respiratory muscles training group (p <0,01). In-hospital mortality and the rate of transfers to the intensive care unit did not differ between groups. The average hospital stay in surviving patients was significantly shorter in main group than in control (14,2±2,5 versus 17,3±2,9 days, p <0,001). Conclusion. Respiratory muscles training with full yogic breathing in addition to standard medical therapy for patients with acute decompensated heart failure leads to a more significant reduction in the severity dyspnea, increased exercise tolerance, improved blood oxygen saturation, and reduced need for diuretics. The use of full breathing is associated with significant improvement in the quality of life and decrease in the length of hospital stay, but does not lead to improvement in hospital outcomes.

Key words: chronic heart failure, decompensation, full yogic breathing, dyspnea, quality of life, diuretics, duration of hospitalization, mortality

#### Conflict of interests

The authors declare no conflict of interests

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Sips-059 ADHF — acute decompensated heart failure, AH — arterial hypertension, CHF — chronic heart failure, FC — functional class, HR — heart rate, LV — left ventricle, 6MWT — 6-minute walk test, RM — respiratory muscles, RR — respiratory rate, SACS — scale for assessing clinical state

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Chronic heart failure (CHF) is one of the most common diseases in the world. Despite the significant progress achieved in recent decades in the management of this pathology, mortality and re-hospitalization rate in patients with CHF remains high. According to information from large registries, currently CHF is found in 26 million people worldwide; its prevalence in the next 30-40 years is expected to increase by 40–60% [1].

Limited physical activity, dyspnea, and fatigue are the main complaints of patients with CHF [2]. For a long time, intracardiac hemodynamics disorders were considered the primary cause of CHF symptoms. It was subsequently demonstrated that there was no clear relationship between the volume and ejection fraction of the left ventricle on the one hand and exercise tolerance on the other [2]. This led to the hypothesis that skeletal muscle weakness makes a crucial contribution to the onset of CHF symptoms [3, 4]. Pathological changes in muscle tissue manifest as systemic vasoconstriction, deterioration of endothelial function, increased myocyte apoptosis, redistribution of the ratio of muscle fibers towards an increase in type II fibers, a decrease in the number and volume of mitochondria, and activation of proinflammatory cytokines. Currently, there are convincing evidences that morphological and functional disorders in muscles accompany CHF course with both reduced and preserved left ventricular (LV) systolic function They lead to excessive neurohumoral activation and are an important factor in worsening the prognosis [5, 6].

Muscle disorders are not limited to motor muscles. The remodeling of the respiratory system plays an essential role in the pathogenesis of CHF. Sarcopenic changes in the diaphragm, increased inspiratory muscle metaboreflex, changes in the sensitivity of pulmonary stretch receptors cause decreased perfusion of respiratory and skeletal muscles, leading to increased dyspnea, decreased exercise tolerance, and deterioration in patients' quality of life.

Aerobic exercise is an important component of the rehabilitation of patients with CHF. Numerous studies in recent years convincingly demonstrated that exercise of various intensity contributes to the improvement of cardiorespiratory parameters, functional ability, vegetative balance, sleep, and quality of life of patients [7–9]. Some studies suggest the positive effect of physical activity on the incidence of cardiovascular events, hospitalizations, and prognosis for patients with CHF [10]. According to the current guidelines [11], aerobic physical activity should be recommended for all patients with CHF, provided they have no contraindications. At the same time, breathing exercise can be an alternative to physical

training for patients with severe decompensated CHF; this is also recommended by current guidelines.

Most often, training respiratory muscles (RM) requires using special devices that create resistance on exhalation or inhalation [11, 12]. However, costs and additional equipment required (often for individual use) limit the practical application of these techniques. Also, elderly patients often have difficulty using these devices due to impaired cognitive and visual functions, preventing them from performing breathing exercises independently. Therefore, there is an urgent need to develop alternative methods of RM training that would not require any additional devices and could be used by a patient at home or in a hospital without involving medical staff. Full yogic breathing could be one of these methods.

Full yogic breathing is a slow, deep breathing that includes three successive phases—abdominal, thoracic, and clavicular. This type of breathing exercise reportedly [13] contributes to increased exercise tolerance, decreased neurovegetative imbalance, and improvement in the quality of life in relatively healthy individuals. However, the study of its effectiveness and safety in patients with CHF has only just started.

This study sought to assess the effectiveness of full yogic breathing in the comprehensive treatment of patients with acute decompensated heart failure (ADHF).

# Material and Methods

Study Design: In a prospective, randomized, open-label, blinded, parallel-group study, 120 patients were enrolled (71 males and 49 females, average age 73.6  $\pm$  5.8 years). Investigators were categorized according to their specific roles in this study: (1) RM training coaches—they teach RM exercises to patients, monitor their execution and do not consider performance; (2) medical evaluators—staff responsible for conducting clinical trial procedures (blinded with respect to groups, but not results); and (3) analysts—responsible for the statistical analysis of the results obtained (blinded with respect to both groups and results).

Inclusion and Exclusion Criteria: The inclusion criteria were the following: age 18+; hospitalization due to ADHF; and consent to participate in the study. The exclusion criteria were the following: treatment in intensive care unit; hemodynamic instability; acute coronary syndrome (ACS)  $\leq$  3 months; percutaneous coronary angioplasty  $\leq$  3 months; coronary artery bypass grafting  $\leq$  3 months; acute cerebrovascular accident  $\leq$  3 months; severe bronchopulmonary pathology; severe gastroesophageal reflux disease, diaphragmatic hernia;

uncontrolled arterial hypertension (AH); life-threatening heart rhythm and conduction disorders; intracardiac thrombosis; acute myocarditis and/or pericarditis; severe valve stenosis; comorbidities in the stage of decompensation; active systemic diseases; malignancies; pregnancy; alcohol and drug addiction; mental illnesses; and inability or unwillingness to comply with the study procedures.

Definition of Inclusion Criteria: CHF was diagnosed in accordance with the criteria recommended by the European Society of Cardiology for the diagnosis and treatment of acute and chronic heart failure in 2016 [14]. ADHF was defined as an acute or gradual buildup in clinical signs and symptoms of hypervolemia (breathlessness, peripheral edema, and pulmonary crackles), which requires additional immediate treatment (intravenous administration of furosemide) and/or hospitalization.

Screening Procedures: Initially, all patients underwent general clinical examination; they were diagnosed with the underlying disease that caused CHF; their comorbidities were analyzed, and the following parameters were assessed: clinical status, quality of life, severity of dyspnea according to the Borg scale, exercise tolerance assessed by 6-minute walk test, and blood oxygen saturation.

Randomization: After the initial examination procedures, all patients were randomized in a 1:1 ratio to a group of breathing exercises performed in addition to standard drug therapy (treatment group, n = 60), or to a group of standard drug therapy only (control group, n = 60). Patients were monitored until they were discharged from the hospital.

End Points: The primary endpoint of this study was the change in dyspnea severity according to a modified Borg scale (modified by V.Yu. Mareev) on Day 7 of treatment. Secondary efficacy variables were the following: changes in clinical status parameters, test distance in 6-minute walk test (6MWT), heart rate (HR), respiratory rate (RR) at rest, and oxygen saturation, quality of life, duration of hospital stay; and hospitalization outcome (discharge, death, or transfer to intensive care unit).

Discharge Criteria: Patients were discharged from the hospital when ADHF symptoms were resolved, euvolemia and stabilization of hemodynamic parameters were achieved, and the renal function and clinical condition of the patient while taking oral medications remained stable for at least the recent 24 hours.

# Study Methods

*Clinical Status:* The clinical status of patients was assessed using the scale for assessing clinical state (SACS) for CHF as modified by V.Yu. Mareev.

6MWT. 6-minute walk test was performed after a 10-minute rest in a sitting position. Patients were advised not to exercise and smoke for 2 hours before the test. For this test, the length of the hospital corridor was measured and a distance of 30 m was defined; chairs were placed at 10-m intervals. The time was counted using a watch with a second hand. The patient was asked to walk in an empty corridor for 6 minutes at his/her own convenient pace, trying to cover the maximum distance. Patients were verbally motivated to perform the exercise twice during the test; current information about the testing phase was also given. Due to significantly reduced exercise tolerance, patients were allowed to take short breaks from walking. The time for forced rest was included in the allocated 6 minutes. In the end, the distance (in meters) covered by the patient in 6 minutes was determined. If such symptoms as chest pain, sudden or severe dyspnea, severe fatigue appeared, 6MWT was stopped.

Severity of Dyspnea: After completing 6MWT, the severity of dyspnea was assessed according to the modified Borg scale.

Quality of Life: The Minnesota Living with Heart Failure Questionnaire was used to assess the quality of life. Patients were asked to answer 21 questions, each related to the factors affecting the quality of life. Patients had to evaluate the effect of any factor on a scale of 0 to 5 depending, on its intensity. The total score was determined at the end of the test: 0 points corresponded to the best quality of life, 105 points—to the worst quality of life.

Pulse Oximetry: Arterial blood oxygen saturation and resting HR were determined by a non-invasive method of percutaneous pulse oximetry using a wrist pulse oximeter (BIOLIGHT CO., LTD, China).

Rate of Fluid Loss: Rate of fluid loss was assessed by measuring body weight daily in the morning in fasting state after emptying the bladder and by calculating the difference between the volumes of fluid consumed and excreted every day.

Drug Therapy: All patients received adequate drug therapy in accordance with the existing standards for CHF management [14]. According to the recommendations, the active phase of diuretic therapy was carried out until physical euvolemia was achieved. Then, the patients were transferred to maintenance diuretic therapy.

Fluid and Electrolyte Balance: During active diuretic therapy, patients were recommended to moderately restrict sodium consumption with food (< 3 g/day) after condition compensation—according to the functional class (FC) of CHF. In the case of CHF FC I, patients were advised not to eat salty food (sodium consumption restriction to 3 g/day), in case of FC II—not to add salt to

food (sodium consumption restriction to 1.5–2 g/day), in case of FC III–IV—use products with low salt content and prepare meals without salt (sodium consumption restriction to 1 g/day). During active diuretic treatment, patients were told to limit fluid intake to 1.5 L/day, after complete compensation of CHF—less than 2 L/day.

The study was completed by 108 patients (53 patients in Group 1 and 55 in Group 2). Twelve subjects discontinued participation in the study: 5 died during their hospital stay, 7 were excluded from the study due to transfer to another department (n = 5) or refusal to participate (n = 2).

RM Training Technique. Patients of the treatment group were trained in the technique of deep yogic breathing, which includes three consecutive phases: abdominal, thoracic, and clavicular. Inspiration was carried out slowly through the nose, in a deep wave-like manner, with the successive involvement of abdominal muscles and the diaphragm, intercostal muscles, and then shoulder girdle muscles. Expiration was carried out in the same sequence. Patients were recommended to breathe as deeply and as slowly as they could tolerate. Participants practiced full breathing in a comfortable sitting position, in a quiet room, at least 3 times every day for 10 minutes under the supervision of an instructor.

Statistical Analysis. Processing was performed on a personal computer using the MedStat statistical analysis software package. At normal distribution, the quantitative characteristics were presented as mean  $\pm$  standard deviation (m  $\pm$   $\sigma$ ), in a case other than normal distribution—as median and 1st, 3rd quartiles (Me (Q1; Q3)). To compare two samples of continuous variables subject to the normal distribution law, paired and unpaired Student's t-tests were used, while the Wilcoxon test was used for other distribution than normal distribution. To compare relative values, we used standard contingency table analysis with the  $\chi^2$  criterion. In all cases of hypothesis testing, differences were considered significant at p < 0.05.

# Results

Initially, both studied groups of patients were comparable in relation to the main clinical and demographic characteristics: gender, age, severity of CHF, and comorbid conditions (Table 1).

In the course of treatment, patients of both groups demonstrated significantly improved parameters of clinical status and exercise tolerance, and decreased severity of dyspnea according to the Borg scale. In the group of breathing exercises, all these changes were more pronounced in comparison with the control group (Table 2).

Changes in the subjective perception of CHF symptoms were accompanied by improved objective

cardiorespiratory parameters. A more pronounced slow-down in HR and RR at rest and improved blood oxygen saturation were observed in patients performing breathing exercises (Table 3).

When comparing the rate of fluid loss, it was found that body weight in patients who performed breathing exercises decreased faster, although there was no difference in the volume of fluid excreted between the groups. The decrease in body weight in the treatment group averaged 0.72  $\pm$  0.06 kg/day, in the control group—0.53  $\pm$  0.06 kg/day (p < 0.001).

Crackles during auscultation were initially heard in 93.1% of patients in the treatment group and in 86.7% of patients in the control group, p > 0.05. In patients practicing full breathing, more rapid regression of the signs of stagnation in pulmonary circulation was observed. On average, pulmonary crackles in the treatment group had stopped by Day 6 from the moment of hospitalization (interquartile interval of 5–7 days), and in the control group—by Day 8 (interquartile interval of 7–9 days), p = 0.024.

We analyzed the duration of the active phase of diuretic therapy and the average dose of the loop diuretic for the entire period of hospitalization. It was revealed that the duration of active diuretic therapy in the treatment group lasted on average 7 days (interquartile range 5-8), in the control group—9 (8-10) days (p = 0.034). The median dose of the loop diuretic during the active phase was significantly (p = 0.003) lower in the treatment group than in the control group, and averaged 60 (40; 80) and 80 (70; 110) mg/day equivalent to furosemide, respectively. During transfer to maintenance treatment, when compensation was achieved, the fixed dose of diuretic was also significantly lower in the treatment group (on average 30 (20; 40) mg/day equivalent to furosemide) in comparison with the control group (on average 40 (30; 60) mg/day), p = 0.018 (Table 4).

During hospitalization, both groups of patients demonstrated notable improvement in the quality of life. However, the improvement was more pronounced in patients practicing full breathing (from  $82.2 \pm 8.6$  to  $62.2 \pm 7.6$  points) compared with the standard therapy group (from  $79.6 \pm 8.4$  to  $69.3 \pm 6.7$  points, p < 0.01).

To assess the effect of full breathing on the course and hospital prognosis of the disease, mortality and the frequency of transfers to the intensive care unit were analyzed (Table 5). In the treatment group, one patient died and two patients were transferred to the intensive care unit, while in the control group, unfavorable outcomes were observed in three and four patients, respectively. The above differences did not reach statistical significance. Nevertheless, the average hospital stay for surviving patients was significantly shorter in the full respiration group than in the standard therapy group.

**Table 1.** Initial clinical characteristics of patients

Parameter	Main group (n=58)	Control group (n=60)	P
BAge, years, Me (Q1; Q3)	73 (66,5; 78)	72 (67; 78,5)	H3/ NS
Male, number of patients (%)	36 (62,1%)	35 (58,3%)	H3/ NS
Arterial hypertension, number of patients (%)	50 (86,2%)	49 (81,7%)	H3/ NS
Myocardial infarction, number of patients (%)	36 (62,1%)	39 (65,0%)	H3/ NS
Atrial fibrillation, number of patients (%)	21 (36,2%)	18 (30,0%)	H3/ NS
Stroke, number of patients (%)	5 (8,6%)	5 (8,3%)	H3/ NS
Chronic obstructive pulmonary disease, number of patients (%)	17 (29,3%)	21 (35,0%)	H3/ NS
Diabetes mellitus, number of patients (%)	23 (39,7%)	21 (35,0%)	H3/ NS
Anemia, number of patients (%)	8 (13,8%)	12 (20,0%)	H3/ NS
NYHA class, Me (Q1; Q3)	III (III; IV)	III (III; IV)	H3/ NS
Signs of fluid retention in two circles of blood circulation, number of patients (%)	51 (87,9%)	48 (80,0%)	H3/ NS
Anasarca, number of patients (%)	7 (12,1%)	5 (8,3%)	H3/ NS
BMI, $kg/m^2$ , $m\pm\sigma$	30,5±3,6	29,4±3,9	H3/ NS
SBP, mmHg, m $\pm \sigma$	131,2±3,9	129,3±4,6	H3/ NS
DBP, mmHg, m±σ	74,9±2,9	76,4±3,2	H3/ NS
Left ventricular ejection fraction %, m $\pm\sigma$	42,8±8,2	44,6±6,2	H3/ NS
Sodium serum level, mmol/l, m $\pm \sigma$	133,5 (132; 137,5)	134,5 (133; 137,5)	H3/ NS
Potassium level, mmol/l, m $\pm\sigma$	4,20±0,36	4,32±0,42	H3/ NS
Blood hemoglobin concentration, g/l m $\pm \sigma$	114,6±7,8	117,3±6,2	H3/ NS
GRF, ml/min, m±σ	44,6±7,9	48,2±8,4	H3/ NS

 $\textbf{Note:} \ \texttt{BMI} - \texttt{body} \ \texttt{mass} \ \texttt{index;} \ \texttt{SBP} - \texttt{systolic} \ \texttt{blood} \ \texttt{pressure;} \ \texttt{DBP} - \texttt{diastolic} \ \texttt{blood} \ \texttt{pressure;} \ \texttt{GRF} - \texttt{glomerular} \ \texttt{filtration} \ \texttt{rate}, \ \texttt{NS} - \texttt{not} \ \texttt{significant} \ \texttt{sig$ 

**Table 2.** Dynamics of clinical status, severity of dyspnea and 6-minute walk test distance  $(M\pm\sigma, Me~(Q1;Q3))$ 

Parameter	Main group		Control group	
	Baseline (n=58)	7th day (n=55)	Baseline (n=60)	7th day (n=53)
Severity of dyspnea according to the Borg scale, score, Me (Q1; Q3)	6 (5; 6)	3 (2; 3)*,#	6 (5; 6)	4 (3; 4)*
Clinical assessment scale, score, Me (Q1; Q3)	9 (8; 10)	4 (3; 5) *,#	8 (8; 10)	6 (5; 7)*
6-minute walk test distance, m, m $\!\pm\!\sigma$	159,4±20,3	209,2±19,6*,#	168,5±22,8	188,6±20,4*

 $\textbf{Note: $^*$- differences are significant (p < 0.05) compared to baseline values, $\#-$ differences are significant (p < 0.05) compared to the control group and the state of the control group are the state of the$ 

**Table 3.** Dynamics of office heart rate, respiration rate and blood oxygen saturation  $(M\pm\sigma, Me\ (Q1;Q3))$ 

	Main group		Control group	
Parameter	Baseline (n=58)	7th day (n=55)	Baseline (n=60)	7th day (n=53)
Respiration rate, at rest, bpm, Me (Q1; Q3)	23 (21; 24)	19 (18; 20)*,#	24 (22; 25)	21 (20; 22)*
HR at rest, bpm, Me (Q1; Q3)	86,8±6,6	72,6±4,8*,#	84,9±6,8	77,4±4,5*
SpO <sub>2</sub> , %	91 (88; 94)	97 (95; 97)* <sup>,#</sup>	90 (88; 92)	94 (93; 96)*

Note: HR — heart rate,  $SpO_2$  — blood oxygen saturation, \* — differences are significant (p<0.05) compared to baseline values, # — differences are significant (p<0.05) compared to the control group

Table 4. Average daily doses of diuretics in terms of furosemide, mg Me (O1; O3)

Therapy phase	Main group (n=58)	Control group (n=60)	P
On the day of hospitalization	80 (80; 120)	80 (70; 110)	p=0,49
Active phase	60 (40; 80)	80 (70; 110)	p=0,003
Maintenance phase	20 (20; 40)	40 (40; 80)	P <0,001

**Table 5.** Hospital outcomes and terms of hospitalization

Parameter	Main group (n=58)	Control group (n=60)	P
Hospital mortality, number of patients (%)	1 (1,72%)	3 (5,00%)	insignificantly
Transfer to the intensive care unit, number of patients (%) (%)	2 (3,44%)	4 (6,67%)	insignificantly
Average terms of hospitalization, days, $m\pm\sigma$	14,2±2,5	17,3±2,9	P <0,001

# Discussion

Respiratory system remodeling plays an important role in the onset of CHF symptoms and disease progression [6, 15]. The diaphragm is a muscle that makes the greatest contribution to ensuring effective gas exchange; it is subject to numerous pathological changes, including increased protein degradation processes, decreased number of mitochondria, and impaired oxidative metabolism. Diaphragm biopsy in patients with heart failure reveals a transition from fast-twitch muscle fibers (type II) to slow-twitch ones (type I), increased apoptosis, and, as a result, replacement of muscle fibers with adipose and connective tissue [16, 17]. This remodeling of RM leads to decreased inspiratory strength and dyspnea [18].

Weakness of RM not only limits the functional capabilities of patients but also exacerbates excessive neuro-humoral activation. Owing to the significant changes in the diaphragm, inspiratory metaboreflex in patients with CHF is activated with slight physical exertion. However, it does not improve gas exchange and cardiac output; it just causes sympathetically mediated vasoconstriction [18, 19]. In turn, a persistent increase in sympathoadrenal activity leads to a further increase in afterload on the

myocardium, closing the vicious circle and worsening the prognosis [20].

RM training is currently regarded as a key rehabilitation measure to ease CHF symptoms and to improve patients' quality of life. Our study demonstrated that the addition of RM training to standard ADHF therapy is associated with a more significant decrease in dyspnea, improved clinical status, increased blood oxygen saturation, and exercise tolerance compared with the standard therapy. Our results are confirmed by other studies. Results of randomized controlled trials in patients with CHF showed that the addition of breathing exercises to aerobic exercise improved cardiovascular response to exercise and its tolerance [21–23]. Experimental models of heart failure demonstrated that training respiratory muscles improved hemodynamic parameters and reduced vegetative disbalance [24].

Mechanisms for implementing the positive effects of breathing exercises vary, and their study is just starting. First of all, they are the result of increasing the reserve of RM. A specific feature of full deep breathing is that during expiration, the diaphragm is pushed up by abdominal muscles, which increases its effectiveness as an inspiratory muscle [24]. By increasing the strength and endurance of respiratory muscles and by increasing the efficiency of

gas exchange, full yogic breathing increases not only the tidal volume but also the saturation of arterial blood with oxygen. This is likely the reason for increased exercise tolerance and reduced dyspnea achieved during this study.

Another mechanism of the effect of breathing exercises is to improve the neurovegetative regulation of cardiovascular and respiratory systems. It is known that CHF course is characterized by a decreased tone of the parasympathetic division of the autonomic nervous system and, therefore, increased activity of its sympathetic division. Hypoxia and hypercapnia that develop in the case of HF activate chemoreceptors in the carotid zone [25]. Signals from these receptors enter the respiratory center in the medulla oblongata and cause the activation of the sympathoadrenal system to maintain adequate blood oxygenation. Increased sympathetic tone primarily manifests as increased respiratory rate, increased systemic blood pressure and HR. There are data on the optimization of the balance of the autonomic nervous system in connection with RM training [26]. By affecting the baroreceptors of lung tissue, as well as stretch receptors located in the smooth muscle layer of large airways, slow deep yogic breathing activates the parasympathetic nervous system and reduces the sensitivity of chemoreceptors [27]. This mechanism is probably responsible for the decrease in HR and RR recorded during this study. A central effect of yogic breathing on the respiratory and vasomotor centers in the medulla oblongata can also not be ruled out. This phenomenon may be based on a network that is common to several respiratory and cardiomotor neurons [28].

We established that full breathing contributes to faster achievement of euvolemia and less need for diuretics. Reducing stagnation is one of the primary goals of treating patients with ADHF. According to current guidelines, intravenous loop diuretics are recommended for patients with no severe arterial hypotension and signs of hypoperfusion immediately after hospitalization. It is recommended to evaluate signs associated with fluid overload on a daily basis (dyspnea, congestive pulmonary crackles, peripheral edema, body weight, and diuresis). We found that body weight in patients who performed breathing exercises decreased faster, although there was no difference in the volume of fluid excreted between the groups. Apparently, full yogic breathing contributed to increased respiratory fluid loss, which explains the more rapid regression of pulmonary congestion in patients of the treatment group [29].

Dyspnea and decreased exercise tolerance in many ways affect the life of patients with CHF. We hypothesized that full breathing, on the contrary, may contribute to a better quality of life. To assess the quality of life, we used the Minnesota Living with Heart Failure Questionnaire; patients were asked to complete it upon admission

and at discharge. During hospitalization, both groups of patients demonstrated notable improvement in the quality of life. However, improvement was more pronounced in patients practicing full breathing compared with the standard therapy group (p < 0.01). The positive effect of breathing techniques on the quality of life was confirmed in many studies [30] and is primarily associated with improved exercise tolerance. Improvement in the psychoemotional state of patients, decreased anxiety, and restoration of breath control can also make a certain contribution to this process [26].

Most studies on RM training did not analyze hard endpoints, that is, survival and cardiovascular event incidence. A distinctive feature of our work was the analysis of the effect of full breathing on the course and hospital prognosis of the disease. We analyzed mortality and the frequency of transfers to the intensive care unit. Full breathing did not lead to an improvement in hospital outcomes. Nevertheless, the average hospital stay in surviving patients was significantly shorter in the full breathing group than in the standard therapy group. It cannot be ruled out that the absence of statistical differences in patient survival is associated with a small sample of patients. Further larger studies are required to investigate this hypothesis.

# Conclusion

Full breathing in addition to standard drug therapy in patients with ADHF leads to a more significant reduction in the severity of dyspnea, increased exercise tolerance, and improved blood saturation. RM exercise contributed to faster regression of pulmonary congestion and the decreased need for diuretics. Full breathing is associated with a significant improvement in patients' quality of life, i.e., more rapid achievement of compensation and shorter hospital stay. However, it does not lead to improvement in hospital outcomes of the disease.

Full yogic breathing is an affordable and relatively easy-to-perform method that does not require additional costs or special equipment. It is important to emphasize that in our study, adherence to breathing exercises increased along with its practice, and patients noted the affordability and effectiveness of this method.

A definite limitation of this study was the lack of blinding with respect to the RM training technique, which, to a certain extent, reduced the validity of the results obtained. Dividing patients into additional subgroups depending on CHF type and severity would help determine the role of full breathing for certain cohorts of patients. Large and well-designed studies to assess the objective determinants of CHF and hard endpoints will help clarify the role of breathing exercises as an important non-pharmacological treatment for CHF.

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# Список литературы/ References:

 Chaudhry S-P., Stewart G.C. Advanced Heart Failure: Prevalence, Natural History, and Prognosis. Heart Fail Clin. 2016; 12(3): 323-333. doi:10.1016/j.hfc.2016.03.001

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- Lalande S., Cross T.J., Keller-Ross M.L. et al. Exercise Intolerance in Heart Failure: Central Role for the Pulmonary System. Exercise and Sport Sciences Reviews. 2020; 48(1): 11-19. doi:10.1249/JES.00000000000000208
- Nakagawa N.K., Diz M.A., Kawauchi T.S. et al. Risk Factors for Inspiratory Muscle Weakness in Chronic Heart Failure. Respir Care. 2020; 65(4): 507-516. doi:10.4187/respcare.06766
- Laoutaris I.D. The "aerobic/resistance/inspiratory muscle training hypothesis in heart failure." Eur J Prev Cardiol. 2018; 25(12): 1257-1262. doi:10.1177/2047487318776097
- Argilés J.M., Busquets S., Stemmler B. et al. Cachexia and sarcopenia: mechanisms and potential targets for intervention.

- Curr Opin Pharmacol. 2015; 22: 100-106. doi:10.1016/j. coph.2015.04.003
- Dos Santos M.R., Saitoh M., Ebner N. et al. Sarcopenia and Endothelial Function in Patients With Chronic Heart Failure: Results From the Studies Investigating Comorbidities Aggravating Heart Failure (SICA-HF). J Am Med Dir Assoc. 2017; 18(3): 240-245. doi:10.1016/j.jamda.2016.09.006
- Okwose N.C., Avery L., O'Brien N. et al. Acceptability, Feasibility and Preliminary Evaluation of a Novel, Personalised, Home-Based Physical Activity Intervention for Chronic Heart Failure (Activeat-Home-HF): a Pilot Study. Sports Medicine — Open. 2019; 5(1): 45. doi:10.1186/s40798-019-0216-x
- Cattadori G., Segurini C., Picozzi A. et al. Exercise and heart failure: an update. ESC Heart Fail. 2018; 5(2): 222-232. doi:10.1002/ehf2.12225
- Oz Alkan H., Uysal H., Enç N. et al. Influence of Breathing Exercise Education Applied on Patients with Heart Failure on Dyspnoea and Quality of Sleep: A Randomized Controlled Study. International Journal of Medical Research & Health Sciences. 2017; 6(9): 107-113
- Belardinelli R., Georgiou D., Cianci G. et al. Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: effects on functional capacity, quality of life, and clinical outcome. Circulation. 1999; 99(9): 1173-1182. doi:10.1161/01.cir.99.9.1173
- 11. Арутюнов Г.П., Колесникова Е.А., Беграмбекова Ю.Л. и др. Рекомендации по назначению физических тренировок пациентам с хронической сердечной недостаточностью. Журнал Сердечная Недостаточность. 2017; 18(1): 41-66. doi:10.18087/rhfj.2017.1.2339

  Arutyunov G.P., Kolesnikova E.A., Begrambekova Yu.L. et al. Exercise training in chronic heart failure: practical guidance of the Russian Heart Failure Society. Russian journal of heart failure. 2017;18(1): 41-66. doi:10.18087/rhfj.2017.1.2339 [In Russian]
- Троицкий М.С., Федоров С.Ю., Борисова О.Н. и др.
  Инновации в тренировке дыхательной мускулатуры
  (литературный обзор). Вестник Новых Медицинских
  Технологий. Электронное Издание. 2015; 2: 3-7.
  doi:10.12737/11911
  Troitsky M.S., Fedorov S.Yu., Borisova O.N. et al. Innovations
  in the training of the respiratory muscles (Literature Review).
  Russian journal of New Medical Technologies. Electronic edition.
  2015; 2: 3-7. [In Russian]
- Udupa K., Madanmohan N., Bhavanani A.B. et al. Effect of pranayam training on cardiac function in normal young volunteers. Indian J Physiol Pharmacol. 2003; 47(1): 27-33.
- 14. Ponikowski P., Voors A.A., Anker S.D. et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2016; 18(8): 891-975. doi:10.1002/ejhf.592

- Saitoh M., Ishida J., Doehner W. et al. Sarcopenia, cachexia, and muscle performance in heart failure: Review update 2016. Int J Cardiol. 2017; 238: 5-11. doi:10.1016/j.ijcard.2017.03.155
- Giallauria F., Piccioli L., Vitale G. et al. Exercise training in patients with chronic heart failure: A new challenge for Cardiac Rehabilitation Community. Monaldi Arch Chest Dis. 2018; 88(3): 987. doi:10.4081/monaldi.2018.987
- Ribeiro J.P., Chiappa G.R., Callegaro C.C. The contribution of inspiratory muscles function to exercise limitation in heart failure: pathophysiological mechanisms. Rev Bras Fisioter. 2012; 16(4): 261-267. doi:10.1590/s1413-35552012005000034
- 18. Boushel R. Muscle metaboreflex control of the circulation during exercise. Acta Physiol (Oxf). 2010; 199(4): 367-383. doi:10.1111/j.1748-1716.2010.02133.x
- 19. Беграмбекова Ю.Л.., Каранадзе Н.А., Орлова Я.А. Нарушения системы дыхания при хронической сердечной недостаточности. Кардиология. 2019; 59(2S): 15-24. doi:10.18087/cardio.2626

  Begrambekova Yu.L., Karanadze N.A., Orlova Y.A. Alterations of the respiratory system in heart failure. Kardiologiia. 2019; 59(2S): 15-24. doi:10.18087/cardio.2626 [In Russian]
- Meyer F.J., Borst M.M., Zugck C. et al. Respiratory muscle dysfunction in congestive heart failure: clinical correlation and prognostic significance. Circulation. 2001; 103(17): 2153-2158. doi:10.1161/01.cir.103.17.2153
- Winkelmann E.R., Chiappa G.R., Camila O.C. Lima. et al.
   Addition of inspiratory muscle training to aerobic training
   improves cardiorespiratory responses to exercise in patients
   with heart failure and inspiratory muscle weakness. Am Heart J.
   2009; 158(5): 768.e1-7. doi:10.1016/j.ahj.2009.09.005
- Stein R., Chiappa G.R., Güths H. et al. Inspiratory muscle training improves oxygen uptake efficiency slope in patients with chronic heart failure. J Cardiopulm Rehabil Prev. 2009; 29(6): 392-395. doi:10.1097/HCR.0b013e3181b4cc41
- 23. Laoutaris I.D., Adamopoulos S., Manginas A. et al. Benefits of combined aerobic/resistance/inspiratory training in patients with chronic heart failure. A complete exercise

- model? A prospective randomised study. Int J Cardiol. 2013; 167(5): 1967-1972. doi:10.1016/j.ijcard.2012.05.019
- Montemezzo D., Fregonezi G.A., Pereira D.A. et al. Influence of inspiratory muscle weakness on inspiratory muscle training responses in chronic heart failure patients: a systematic review and meta-analysis. Archives of Physical Medicine and Rehabilitation. 2014; 95(7): 1398-1407. doi:10.1016/j. apmr.2014.02.022
- 25. Passino C., Giannoni A., Milli M. et al. Recent knowledges on chemosensitivity to hypoxia and hypercapnia in cardiovascular disease. Recenti Prog Med. 2010; 101(7-8): 308-313.
- 26. Novaes M.M., Palhano-Fontes F., Onias H. et al. Effects of Yoga Respiratory Practice (Bhastrika pranayama) on Anxiety, Affect, and Brain Functional Connectivity and Activity: A Randomized Controlled Trial. Front Psychiatry. 2020; 11: 467. doi:10.3389/fpsyt.2020.00467
- 27. Shinba T., Inoue T., Matsui T. et al. Changes in Heart Rate Variability after Yoga are Dependent on Heart Rate Variability at Baseline and during Yoga: A Study Showing Autonomic Normalization Effect in Yoga-Naïve and Experienced Subjects. Int J Yoga. 2020; 13(2): 160-167. doi:10.4103/ijoy.IJOY\_39\_19
- Garcia A.J., Koschnitzky J.E., Dashevskiy T. et al.
   Cardiorespiratory Coupling in Health and Disease. Auton Neurosci. 2013; 175(0): 26-37. doi:10.1016/j.autneu.2013. 02.006
- 29. Покровский В.М., Коротько Г.Ф. Физиология человека. 2003; 656 с. [Электронный ресурс]. URL: https://www.booksmed. com/fiziologiya/565-fiziologiya-cheloveka-pokrovskij-uchebnik. html. (дата обращения: 12.06.2020). Pokrovskiy V.M., Korotko G.F. Human physiology. 2003; 656 p. [Electronic resource]. URL: https://www.booksmed. com/fiziologiya/565-fiziologiya-cheloveka-pokrovskij-uchebnik. html. (Date of the application: 12.06.2020) [In Russian]
- 30. Smart N.A., Giallauria F., Dieberg G. Efficacy of inspiratory muscle training in chronic heart failure patients: a systematic review and meta-analysis. Int J Cardiol. 2013; 167(4): 1502-1507. doi:10.1016/j.ijcard.2012.04.029