



comparative study of the correlation between pulmonary artery systolic pressure and central hemodynamic parameters and treatment efficacy in patients with chronic obstructive pulmonary disease with pulmonary hypertension.

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Abstract:

According to scientists from the European Respiratory and American Thoracic Society, only 25% of cases of chronic obstructive pulmonary disease (COPD) are diagnosed in time. In the remaining cases, the disease is diagnosed as a result of pulmonary hypertension (PH), followed by the development of chronic pulmonary-cardiac syndrome (CPCS). The first scientific study to assess the condition of the left ventricle (LV) in patients with COPD was conducted in the 80s and 90s, in which mainly interventional methods were used in experimental models. According to a number of recent studies, diastolic dysfunction of the heart is detected in 50-90% of patients with COPD. This article shows that cardiac hemodynamic parameters in patients with chronic obstructive pulmonary disease with pulmonary hypertension change negatively in parallel with the severity of the disease.

Key words: chronic obstructive pulmonary disease (COPD), pulmonary hypertension (PPH), systolic pressure in the pulmonary artery (SPPA), left ventricle of heart (LV).

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Introduction

Chronic obstructive pulmonary disease (COPD) is a process characterized by a sharp decrease in airflow in the lungs and airways and the activation of chronic inflammatory processes in response to harmful particles or gases. is one of the current problems of medicine with possession. According to official data from the World Health Organization (WHO), about 600 million people worldwide are diagnosed with COPD. Today, about 40% of the total deaths among the population of developed countries are caused by this disease. [6; 11; 12; 13; 16; 18]. Nearly 3 million patients die each year from the disease. A study by Minino and co-authors (2011) found that in the United States, 377 patients died per day from COPD, a higher rate of death from myocardial infarction [19]. At the same time, the disease is costly and costs \$ 40 billion in the United States during its outbreak.[8]

According to scientists from the European Respiratory and American Thoracic Society, in only 25% of cases, COPD is detected

in time. In the remaining cases, the disease is diagnosed as a result of pulmonary hypertension (PH), followed by the development of chronic pulmonary heart disease (CPHD) [1; 2; 20].

According to recent data, OG, which develops due to lung disease or hypoxemia, is the second most prevalent, ie after its secondary form, which develops due to pathology of the left side of the heart [3].

The first scientific study to assess the condition of the left ventricle (CV) in patients with COPD was conducted in the 80s and 90s, in which mainly interventional methods were used in experimental models [5]. A number of recent studies have shown that diastolic dysfunction of the heart is detected in 50-90% of patients with OCD [10; 14; 17]. There are very few data on systolic dysfunction in the course of the disease, and the continuation of scientific research in this area is one of the most pressing issues in modern medicine [7; 9; 21].

Purpose, materials and methods of inspection

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Taking into account the above, we took as a research source 120 patients with mixed pulmonary hypertension of the ICU in the Bukhara Regional Multidisciplinary Hospital and treated in the hospital. Their clinical functional examinations were conducted in accordance with the guidelines of the [Eurasian Clinical Recommendation for the Diagnosis and Treatment of Pulmonary Hypertension (2019)] in line with the latest international program. They identified the functional class of pulmonary hypertension by objective

examination, generally accepted laboratory-instrumental, including ECHOCG.

In classifying patients into functional classes, not only clinical signs but also indicators of external respiratory activity were taken into account.

Table 1 below shows the distribution of patients by age, sex, disease type, and severity. In determining the types of ICU, patient complaints were based on the results of objective examination, clinical-instrumental and laboratory tests.

1-table

Clinical functional classification of patients with chronic obstructive pulmonary disease and involved in the study

Information on the patients and disease types studied	Chronic obstructive pulmonary disease complicated by pulmonary hypertension Functional class II (moderate to severe) $50\% \leq 1REV < 80$		Chronic obstructive pulmonary disease complicated by pulmonary hypertension Functional class III (severe course) $30\% \leq 1REV < 50$		Chronic obstructive pulmonary disease uncomplicated with pulmonary hypertension Functional class IV (very severe) $1REV < 30$	
	n=40		n=40		n=40	
	abs.	%	abs.	%	abs.	%
Men	23	57.5	23	57.5	19	47.5
Women	17	42.5	17	42.5	21	52.5
Age	53.05±2.65		56.27±2.85		64.12±2.255	
Mixed type	40	100	40	100	40	100

Илюба: 1REV- 1 rapid expiratory volume per second (in this and in tables and in the text).

The following groups of drugs were selected as the standard treatment of COPD in patients with the severity of the disease, depending on the period of exacerbation and remission: bronchodilators (b2 agonists, M-cholinolytics, methylxanthines), hormones by inhalation and antibiotics in similar doses.

The first group in our follow-up consisted of 40 patients with chronic obstructive pulmonary disease complicated by pulmonary hypertension with functional class II, with a mean age of 53.05 ± 2.65 . 57.5% of them are men and 42.5% are women. This group, in turn, was divided into two subgroups of 20 each, based on the recommended treatments.

The first subgroup of patients received bosentan 62.5 mg 2 times a day and eplerenone 25 mg once a day based on the recommended complex treatment based on their general condition and laboratory functional parameters. Their mean age was 53.05 ± 0.65 , with 55% males and 45% females.

The second subgroup of patients received seldinafil 25 mg once a day and eplerenone 25 mg once a day based on the recommended complex treatment based on their general condition and laboratory functional parameters. Their mean age was 53.05 ± 2.65 , with 60% males and 40% females.



Chronic obstructive pulmonary disease complicated by pulmonary hypertension was functional class III, i.e., the second group also included 40 patients, with an average age of 56.27 ± 2.85 , comprising 57.5% of men and 42.5% of women. This group, in turn, was divided into two subgroups of 20 each, based on the recommended treatments. The first subgroup of patients with chronic obstructive pulmonary disease received 125 mg of bosentan 2 times a day and 50 mg of eplerenone once a day on the basis of the recommended complex treatment based on laboratory functional indicators. Their mean age was 57.25 ± 2.59 , with 55% males and 45% females. The second subgroup of patients with chronic obstructive pulmonary disease received seldinafil 50 mg once a day and eplerenone 50 mg once a day in the morning on the basis of the recommended complex treatment based on laboratory functional indicators. Their mean age was 55.3 ± 3.1 , with 60% males and 40% females.

Chronic obstructive pulmonary disease complicated by pulmonary hypertension of the third group consisted of 40 patients with functional class IV, with an average age of 64.12 ± 2.255 , with 47.5% men and 52.5% women. This group, in turn, was divided into two subgroups of 20 each, based on the recommended treatments. The first subgroup of patients with chronic obstructive pulmonary disease received bosentan 125 mg 2 times a day and eplerenone 100 mg once a day based on the recommended complex treatment based on laboratory functional indicators. Their average

age was 65.25%, with 50% males and 50% females. In the second subgroup of patients with chronic obstructive pulmonary disease, the general condition of the patient received seldinafil 50 mg once a day and eplerenone 100 mg once a day in the morning on the basis of the recommended complex treatment based on laboratory functional indicators. Their mean age was 63.1 ± 1.4 , with 45% males and 55% females.

Echocardiography (EchoCG) was performed in a transthoracic manner on a Vivid S60N device (NORWAY) with a 3.5 MHz sensor. In order to ensure a clear view of the structural structure of the heart in different positions of the patient, M and V pulse wave dopplerography was performed in accordance with the recommendations of the American Echocardiography Association (ASE).

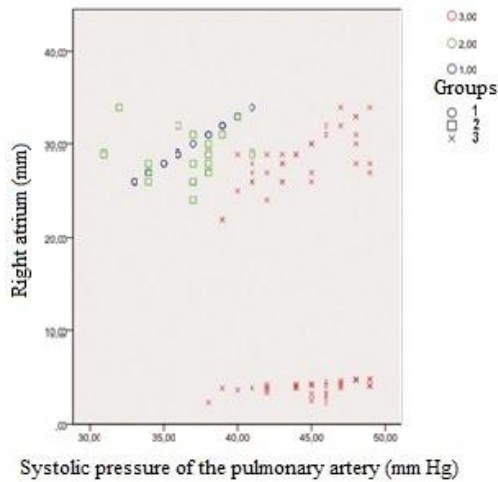
We studied the degree of correlation of a number of hemodynamic parameters with the systolic pressure of the pulmonary artery when different degrees of severity of COPD were associated with pulmonary hypertension.

Results and analysis

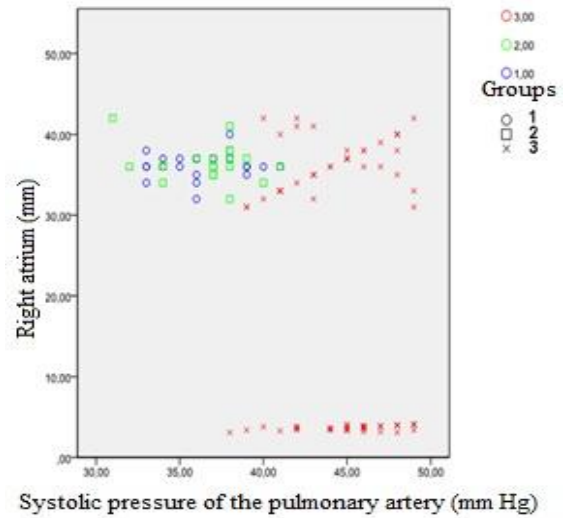
In our follow-up, a reliable positive correlation ($r = 0.4$; $P < 0.01$) was found between pulmonary artery systolic pressure (RAS) and right ventricular size in patients diagnosed with stage II COPD and pulmonary hypertension. In stage III of the disease, these values were $r = 0.7$ and $P < 0.01$, respectively. A reliable positive correlation ($r = 0.35$; $P < 0.02$) was also noted between the OSA and the right subdivision at this stage.



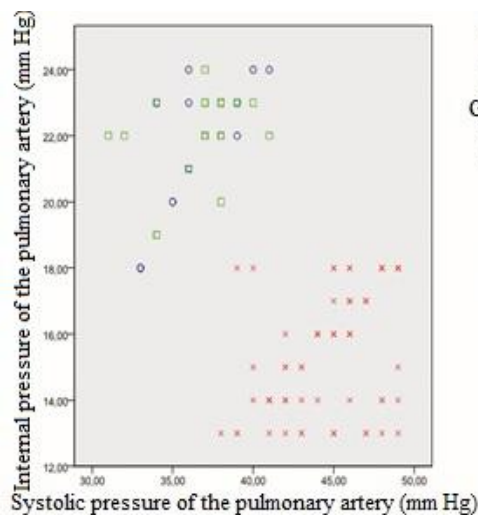
In cases with stage IV pulmonary hypertension, $r = 0.52$, respectively, between the right ventricle and the right ventricle with OSA; $P < 0.001$ and $r = 0.47$; A reliable correlation of $p < 0.002$ was found (Figures 1 and 2). These indicators show an increase in the size of the right side of the heart in parallel with the increase in pressure in the pulmonary artery and the transition to the severe stage of COPD.



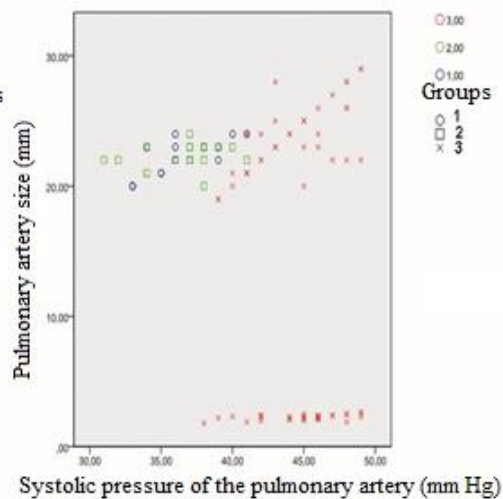
1 расм. Ўпканинг сурункали обструктив касаллиги турли оғирлик даражаларида кечганда ўпка артериясининг систолик босими билан ўнг қоринча орасидаги корреляцион боғлиқлик.



2 расм. Ўпканинг сурункали обструктив касаллиги турли оғирлик даражаларида кечганда ўпка артериясининг систолик босими билан ўнг бўлмача орасидаги корреляцион боғлиқлик.



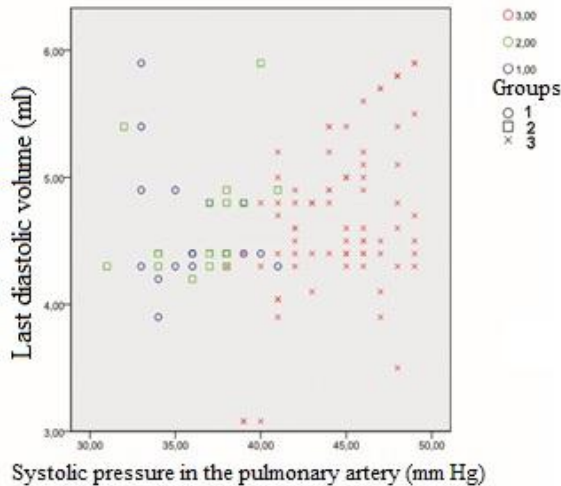
3 graph. A correlation between the systolic pressure of the pulmonary artery and the internal pressure of the pulmonary artery when chronic obstructive pulmonary disease occurs at different severity.



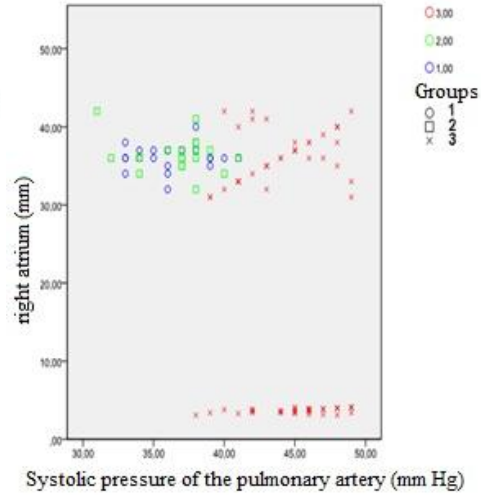
4 graph. A correlation between systolic pressure of the pulmonary artery and pulmonary artery size when chronic obstructive pulmonary disease occurs at different severity.



In addition to the above, COPD II was associated with pulmonary artery measurement ($r = 0.4$; $P < 0.006$) and pulmonary artery internal pressure (pulmonary artery pressure after valve closure) ($r = 0.4$; $P < 0.003$) A positive correlation was noted. At the severity level of COPD III, these indicators were observed more reliably ($r = 0.68$; $P < 0.001$ and $r = 0.49$; $P < 0.001$, respectively).



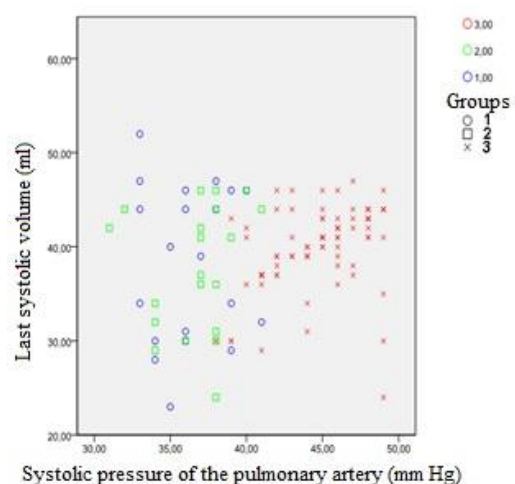
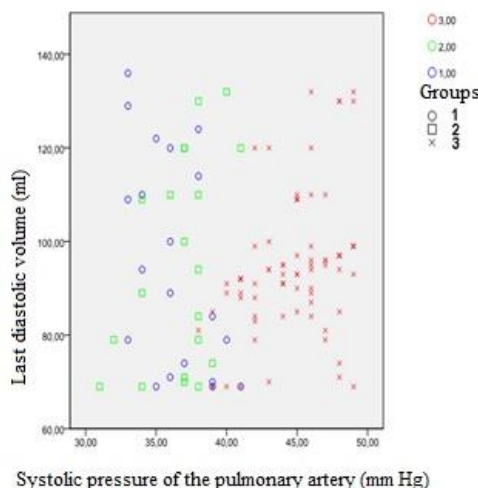
5 graph. Correlation between systolic pressure of the pulmonary artery and end-diastolic measurement when chronic obstructive pulmonary disease occurs at different severity.



6 graph. A correlation between the systolic pressure of the pulmonary artery and the final systolic size when chronic obstructive pulmonary disease occurs at different severity.

In addition, in patients with stage IV disease under observation, a positive correlation between COPD and pulmonary artery internal pressure and pulmonary artery diameter ($r = 0.37$; $P < 0.01$ and $r = 0.59$; $P < 0.001$, respectively) was observed in the pulmonary artery. confirms the passage in common (Figures 3 and 4).

Most of the literature focuses on changes in the right side of the heart in pulmonary hypertension.



7 graph. Correlation between systolic pressure of the pulmonary artery and end-diastolic volume when chronic obstructive pulmonary disease occurs at different severity.

8 graph. A correlation between the systolic pressure of the pulmonary artery and the final systolic volume when chronic obstructive pulmonary disease occurs at different levels of severity.

In our observation, the severity of COPD IV in patients with pulmonary hypertension was determined not only by the right ventricular ($r = 0.5$; $P < 0.001$), but also by the final diastolic ($r = 0.47$; $P < 0.002$) and systolic measurement ($r = 0.59$; $P < 0.001$) and a positive correlation between the last diastolic ($r = 0.55$; $P < 0.001$) and systolic volume ($r = 0.39$; $P < 0.01$). confirms (Figures 5 and 6 and Figures 7 and 8).

It is known that one of the changes observed in the cardiovascular system in COPD is right ventricular and ventricular dysfunction, and pulmonary hypertension develops. However, in the available literature, very little attention has been paid to changes in the left ventricle when COPD is associated with pulmonary hypertension. In addition, we did not find a comparative study of the effects on the hemodynamics of the heart when co-administered sildenafil with eplerenone, a typical representative of the endothelin receptor antagonist - usenta 125 (bosentan) and type 5 phosphodiesterase group in this group of patients. With this in mind, all patients with COPD and pulmonary hypertension in our study were divided into groups based on their severity and the recommended complex treatment, and intracardiac hemodynamics were assessed. The first group consisted of 40 patients with COPD II functional class (severity) who had pulmonary hypertension and were studied in two subgroups based on standard treatment. The first subgroup consisted of 20 patients receiving bosentan and eplerenone on the basis of standard treatment, and the second group of 20 patients received eplerenone with sildenafil (Table 2).

2-table

Peripheral blood pressure and echocardiography before and after treatment of chronic obstructive pulmonary disease with functional class II pulmonary hypertension.

№	Indicators	Chronic obstructive pulmonary disease complicated by pulmonary hypertension Functional class II n =40				
		Standard treatment bozentan +eplerenone n = 20		The standard treatment with sildenafil eplerenonen=20		The degree of reliability of the difference between the two groups after treatment (P)
		Before treatment	After treatment	Before treatment	After treatment	
1	Systolic arterial blood pressure (mm. Hg. col.)	130±3,2	118,6±1,89* **	132±3,4	120,25±1,79* **	P>0,05
2	Diastolic arterial blood pressure (mm.Hg.col)	82,75±1,57	75,72±1,22* **	79,6±2,4	78,7±1,05	P<0,05
3	Average arterial blood pressure	98,5±1,7	92,55±0,86* **	97,07±2,7	92,55±0,86	P>0,05



	(mm.Hg.col)					
4	Left atriummm)	35.2 ±1.2	33.9 ±1.2	35.5±1.0 4	34.3±1.04	P>0,05
5	Right atriem(mm)	36.45±0.5	33.45±0.5** *	36.05±0. 36	35.1±0.37	P<0,001
6	Right ventricle(mm)	28.6±0.57	26.6±0.56*	29.25±0. 56	27.4±0.54	P>0,05
7	Last systolic volume (ml)	37.75±1.5	35.85±1.5	38.3±1.8 5	36.4±1.85	P>0,05
8	Last diastolic volume (ml)	94.9±4.99	92.9±4.99	95.5±5.1 4	93.6±5.17	P>0,05
9	Last systolic measurement (sm)	2.9±0.064	2.6±0.064**	2.83±0.0 8	2.75±0.09	P<0,05
10	Last diastolic measurement (sm)	4.6± 0.09	4.3± 0.09*	4.58±0.1 0	4.39±0.10	P<0,05
11	Pulmonary artery (mm)	22.35±0.20	20.65±0.19* **	22.15±0. 31	21.65±0.19**	P<0,001
12	Systolic pressure in the pulmonary artery (mm.Hg.col)	36.7±0.56	27.7±0.56** *	36.25±0. 65	30.9±0.68***	P<0,001
13	Left ventricular ejection fraction (%)	61.1±1.16	64.4±1.16	62.1±1.1 6	64.2±1.16	P>0,05

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Systolic blood pressure decreased reliably after treatment in both subgroups, respectively (130 ± 3.2 mm Hg and 118.6 ± 1.89 mm Hg, $P < 0.001$ and 132 ± 3.4 mm Hg, respectively. sim. ust. and 120.25 ± 1.79 mm. sim. ust).

Diastolic and mean blood pressure readily decreased significantly in the group receiving bosentan after treatment alone after treatment ($P < 0.001$, Table 2). This indicates that bosentan has a high hypotensive effect compared to sildenafil.

Echocardiographic examinations revealed that in the first subgroup, the size of the left ventricle was 35.2 ± 1.2 mm and 33.9 ± 1.2 mm after treatment. In the second subgroup, these numbers were 35.5 ± 1.0 mm and 34.3 ± 1.0 mm, respectively, and no reliable changes were observed in both subgroups after treatment ($P > 0.05$). After the treatments, the rates in the first subgroup decreased by 3.6% and in the second subgroup by 3.4%, and the difference between them (0.2%) was unreliable ($P > 0.05$).

The size of the right ventricle ranged from 36.45 ± 0.5 mm to 33.45 ± 0.5 mm, respectively, before and after treatments in the first subgroup. decreased, the difference between them was 8.2%, and a reliable ($P < 0.001$) change was observed. In the second subgroup, these numbers were 36.05 ± 0.36 and 35.1 ± 0.37 mm, respectively, with a pre-treatment difference of 2.5% unreliable ($P > 0.05$). Postoperative rates were 5.7% higher in the first subgroup than in the second, and the differences were reliable ($P < 0.01$).

The right ventricular size was 28.6 ± 0.57 mm and 26.6 ± 0.56 mm, respectively, before and after treatments in the first subgroup. and decreased reliably by 7% ($P < 0.05$). In the second subgroup, these numbers were 29.25 ± 0.54 and 27.4 ± 0.5 mm, a decrease of 3.5%, and the differences were unreliable



($P > 0.05$). The difference between the two subgroups was 3.49%, and although the former did not differ reliably from the latter, the figures were significantly higher.

This confirms that bozentan when used in combination with eplerenone has a positive effect not only on the right ventricle, but also on the right ventricular hemodynamic parameters.

The final systolic volume was 37.75 ± 1.5 and 35.85 ± 1.5 ml, respectively, before and after treatment in the first subgroup, and the differences were 5% ($P > 0.05$). In the second subgroup, the values were 38.3 ± 1.85 and 36.4 ± 1.8 ml, respectively, and the difference between the pre- and post-treatments was 4.96% ($P > 0.05$). The difference between the two subgroups was 0.04% after the treatments and it was confirmed that the indicators did not differ from each other reliably ($P > 0.05$).

The last diastolic volume before and after treatment in the first subgroup was 94.9 ± 4.99 and 92.9 ± 4.99 ml, respectively, and in the second subgroup 95.5 ± 5.14 and 93.6 ± 5.17 ml, respectively. In this case, the difference in the first subgroup was 2.1% and in the second subgroup was 2.0%, and the changes after treatment did not differ significantly from each other in both groups and were equal to 0.1% ($P > 0.05$).

A comparative analysis showed that bozentan and sildenafil had similar effects on end-diastolic and systolic volume in small groups with eplerenone. However, in both groups, these figures were unreliable ($P > 0.05$).

The last systolic measurement in the first subgroup was 2.9 ± 0.06 cm and 2.6 ± 0.06 cm, respectively, before and after the treatments. The difference between them was 10.3%. In the second subgroup, these values were 2.83 ± 0.08 cm and 2.75 ± 0.09 cm, respectively, before and after treatment, no difference was detected. In the small group receiving the first bozentan and eplerenone, the final systolic measurement decreased reliably by 10.3% after treatment ($P < 0.001$).

The last diastolic measurement was 4.6 ± 0.09 and 4.3 ± 0.09 cm, respectively, before and after treatment in the first subgroup, and the difference between them was reliable ($P < 0.05$). In the second subgroup, however, the differences were unreliable ($P > 0.05$) after treatment, with 4.58 ± 0.1 and 4.39 ± 0.1 , respectively. Post-treatment rates were 6.5% positive in the first subgroup and 4.1% positive in the second. These changes differed in the first subgroup with high reliability ($P < 0.05$) compared to the second (2.4%). This indicates a significant decrease in end-diastolic measurement when bozentan is used in combination with eplerenone.

The diameter of the pulmonary artery was 22.35 ± 0.19 mm before treatment and 20.65 ± 0.19 mm after treatment, respectively, in a small group receiving bozentan and eplerenone on the basis of the first, i.e., COPD standard treatment. and the differences were 8.8% ($P < 0.001$). In the second group, i.e., sildenafil and eplerenone, the values were 22.15 ± 0.2 and 21.65 ± 0.1 mm, respectively, before and after the treatments. formed. Pre- and post-treatment rates were 4.4% in this group, and the differences were reliable ($P < 0.001$). In addition, the first group post-treatment index was 4.4% higher than that of the second group, confirming that bozentan had a reliable ($P < 0.001$) lowering effect on pulmonary artery pressure from sildenafil.

Also, in the small group receiving bozentan, the difference in postoperative systolic pressure in the pulmonary artery was 28.4% positive (36.7 ± 0.56 and 27.7 ± 0.56 mm Hg, respectively) relative to the previous value ($P < 0.001$).). In the group receiving sildenafil, it was 19.6% ($P < 0.001$) (36.25 ± 0.65 and 30.9 ± 0.68 mm.sim.ust., Respectively). The difference between the postoperative groups was 8.8% higher in the first group than in the second group ($P < 0.001$), indicating that bozentan had a higher positive effect on pulmonary artery pressure reduction than sildenafil.

In both subgroups, left ventricular hemorrhage fractions were evaluated before and after treatments. In the first subgroup, the values were $61.1 \pm 1.16\%$ and $64.4 \pm 1.0\%$, respectively (difference 5.4%, $P > 0.05$), and in the second subgroup $62.1 \pm 1.1\%$ and $64.2 \pm 1.0\%$ (difference 3.38%, $P > 0.05$). The difference in positive changes between the groups after treatment was 2.02%, and the



indicators were not reliable ($P > 0.05$). In both subgroups, the heart rate fraction changed positively after the treatments, but they did not differ significantly from each other. However, the effect of bosentan on it was confirmed to be higher than that of sildenafil.

The second group consisted of 40 patients with COPD III functional class (severity) who had pulmonary hypertension. They, in turn, were divided into two subgroups of 20 each, as in the first group, based on the recommended treatments (Table 3). **Table-3**

Peripheral blood pressure and echocardiography indicators before and after treatment in patients with chronic obstructive pulmonary disease class III with pulmonary hypertension.

№	Indicators	Peripheral blood pressure and echocardiography indicators before and after treatment in patients with chronic obstructive pulmonary disease class III with pulmonary hypertension. n =40				
		Standard treatment bozentan +eplerenone n = 20		The standard treatment with sildenafil eplerenonen=20		The degree of reliability of the difference between the two groups after treatment (P)
		Before treatment	After treatment	Before treatment	After treatment	
1	Systolic arterial blood pressure (mm. Hg. col.)	138,25±2,46	122,5±1,38**	140,0±3,06	129,55±1,5***	P<0,001
2	Diastolic arterial blood pressure (mm.Hg.col)	85,5±1,4	78 ±1,1***	82,75±1,93	80,5±1,14*	P<0,001
3	Average arterial blood pressure (mm.Hg.col)	103,08±1,7	92,8±1,1***	102,83±2,28	96,85±1,1***	P<0,001
4	Left atrium mm)	34.4±0.81	31.3±0.8*	33.15±0.6	31.8±0.6	P>0,05
5	Right atriem(mm)	41.6±0.43	38.6±0.44*	42.8±0.43	40.9.±0.4	P<0,001
6	Right ventricle(mm)	37.25±0.69	34.25±0.7*	38.25±0.7	36.±0.7	P>0,05
7	Last systolic volume (ml)	40.05±1.35	36.05±1.5	38.75±0.91	32.05±0.5	P<0,05
8	Last diastolic volume (ml)	94.9±4.99	92.9±4.99	99.4±3.86	92.75±0.7	P>0,05
9	Last systolic measurement (sm)	3.14±0.11	2.57±0.06**	3.52±0.11	3.12±0.13	P<0,001
10	Last diastolic measurement (sm)	4.39±0.06	4.2±0.06**	4.51±0.17	4.34±0.18***	P>0,05



11	Pulmonary artery (mm)	23.85±0.53	21.8±0.53*	23.2±0.6 7	22.25±0.6	P>0,05
12	Systolic pressure in the pulmonary artery (mm.Hg.col)	44.75±0.65	28.05±0.55* **	43.22±0. 67	30,7±0.56***	P<0,05
13	Left ventricular ejection fraction (%)	61.2±1.16	64.2±1.16	62.2±1.1 5	64.1±1.16	P>0,05

In both subgroups in this group, systolic, diastolic, and mean arterial blood pressure readings decreased reliably ($P < 0.001$) after treatment. However, when blood pressure readings were compared between groups after treatment, it was noted that in the first subgroup its propensity to decrease was significantly higher than in the second subgroup ($P < 0.001$).

Echocardiographic examination of preoperative and postoperative subjects revealed the following. In the first subgroup, the left ventricle size varied from 34.4 ± 0.81 to 31.3 ± 0.8 mm, decreased by 9.6%, and the differences were reliable ($P < 0.05$). In the second subgroup, these values were 33.15 ± 0.6 mm before treatment and 31.8 ± 0.6 mm after treatment, respectively, and decreased by 4.0% ($P > 0.05$). The difference between the two subgroups was 5.6% higher in the first subgroup after treatment than in the second subgroup after treatment, but no reliable difference was observed between them. ($P > 0.05$).

The right subgroup values in both subgroups before and after treatment were 41.6 ± 0.43 and 38.6 ± 0.44 mm, respectively, with a difference of 8.1% reliable ($P < 0.05$) and 42.8 ± 0.43 and 40.9 ± 0.4 mm, a change of 2.9%, but in the end the figure was unreliable ($P > 0.05$). A comparison between the two subgroups confirms that after the treatments, reliable ($P < 0.001$) changes were observed in the first subgroup, which was 5.2% higher than in the first subgroup, and that bosentan had a positive effect on right subclinical measurements relative to sildenafil.

The size of the right ventricle in the first subgroup was 37.25 ± 0.56 and 34.25 ± 0.7 mm before and after the treatments, respectively. decreased reliably by 7% ($P < 0.05$). In the second subgroup, these values were 38.25 ± 0.7 and 36.0 ± 0.7 mm, decreasing by 2.2%, and the differences were unreliable ($P > 0.05$). The difference in the first subgroup after treatment was 4.8% higher than in the second subgroup, confirming that the right ventricular size was reliably reduced ($P < 0.05$) after the treatments in the group receiving bosentan.

In the first subgroup receiving bosentan and eplerenone, the final systolic volume before and after the treatments was 40.05 ± 1.5 and 36.05 ± 1.5 ml, respectively, differing by 4.5% and was unreliable ($P > 0.05$). In the second subgroup of sildenafil and eplerenone recommended, the values were 38.75 ± 0.91 and 32.05 ± 0.5 ml, respectively, and the differences were 3%. When comparing the differences between the two groups, the final systolic volume readings in the first group were more reliable than in the second group ($P < 0.05$). decreased.

The last diastolic volume in the first subgroup before and after the treatments was 94.9 ± 4.99 ml and 92.9 ± 4.99 ml, respectively, with a difference of 2.1%. In the second subgroup, 99.4 ± 3.86 and 92.75 ± 0.7 ml were administered before and after the treatments, respectively, and the difference between them was 1%. When the post-treatment parameters of the two groups were compared, they did not differ significantly from each other.

Recent systolic measurements were also 3.14 ± 0.11 cm before treatment in the first subgroup and 2.57 ± 0.06 cm after treatment, and the differences were 10.4% and varied reliably ($P < 0.001$). In the second subgroup, the readings were 3.52 ± 0.11 and 3.12 ± 0.13 cm, respectively, with a 4.4% decrease in recent systolic measurement, but the difference between them was unreliable ($P > 0.05$).



When the difference between the two subgroups was compared, the rate was 6.4%, and in the subgroup receiving bosentan, the final systolic size decreased reliably relative to the second subgroup ($P < 0.001$).

The last diastolic measurement was 4.39 ± 0.06 and 4.2 ± 0.06 cm ($P < 0.001$) and 4.51 ± 0.17 and 4.34 ± 0 , respectively, in the first and second subgroups before and after treatment. 18 cm ($P < 0.001$), and the differences after treatment were 4.3% and 2.2%, respectively. The difference between the two groups was 2.1% after treatment ($P > 0.05$).

The diameter of the pulmonary artery in the first subgroup before and after treatment was 23.85 ± 0.53 and 21.8 ± 0.53 mm, respectively. (difference 3.6%, $P < 0.05$), and in the second subgroup 23.2 ± 0.67 and 22.25 ± 0.6 mm, respectively. (difference 5.3%, $P > 0.05$) and the differences between the two groups were not reliable ($P > 0.05$).

The systolic pressure in the pulmonary artery in the first subgroup increased from 44.75 ± 0.65 to 28.05 ± 0.55 mm.sim.ust or 23.4% ($P < 0.001$), and in the second subgroup it was 43.22. Decreased from ± 0.67 to 30.7 ± 0.56 mm.sim.ust i.e. 15.3% reliable ($P < 0.001$). However, mean pulmonary artery pressure was found to be 8.0% reliable ($P < 0.05$) lower in the first subgroup receiving bosentan eplerenone than in the second.

In both subgroups, left ventricular hemorrhage fractions were evaluated before and after treatments. In the first subgroup, the values were $61.2 \pm 1.16\%$ and $64.2 \pm 1.16\%$, respectively (difference 4.6%, $P > 0.05$), and in the second subgroup $62.2 \pm 1.1\%$ and $64.1 \pm 1.16\%$ (difference 2.96%, $P > 0.05$). In both subgroups, the heart rate fraction changed positively after the treatments, but they were not reliable. However, the effect of bosentan on it was confirmed to be higher than that of sildenafil.

The third group consisted of 40 patients with COPD IV functional class (severity) of pulmonary hypertension. They, in turn, were divided into two subgroups, each of 20, as in the above groups, based on the recommended treatments (Table 4).

Table-4

Peripheral blood pressure and echocardiography indicators before and after treatment in patients with chronic obstructive pulmonary disease class IV pulmonary hypertension.

№	Indicators	Chronic obstructive pulmonary disease complicated by pulmonary hypertension Functional class IVn =40				
		Standard treatment bozentan +eplerenone n = 20		The standard treatment with sildenafil eplerenonen=20		The degree of reliability of the difference between the two groups after treatment (P)
		Before treatment	After treatment	Before treatment	After treatment	
1	Systolic arterial blood pressure (mm. Hg. col.)	148,4±2,2	122,5±1,3** *	146,1±2,2	139,8±2,2***	P<0,001
2	Diastolic arterial blood pressure (mm.Hg.col)	91,3±1,25	78±1,11***	90,05±1,4	85,2±1,2***	P<0,001
3	Average arterial blood pressure	110,3±1,4	92,83±1,12* **	108,7±1,57	103,4±1,4***	P<0,001



	(mm.Hg.col)					
4	Left atrium mm)	34,05±0,56	32,1±0,51*	37,05±0,54	32,1±0,56	P>0,05
5	Right atriem(mm)	3.6±0.06	3.3±0.06*	3.5±0.06	3.4±0.06	P>0,05
6	Right ventricle(mm)	3,7±0.1	2.5±0.06***	3,9±0.04	3,08±0.08***	P<0,001
7	Last systolic volume (ml)	41±0,4	31±0.4***	39,4±1,05	32,4±0,6***	P>0,05
8	Last diastolic volume (ml)	90.9±1.16	86.05±1.26*	92.85±1.28	89.6±1.2**	P<0,05
9	Last systolic measurement (sm)	3,01±0,11	2,7±0,11	2,93±0,11	2,36±0,14	P>0,05
10	Last diastolic measurement (sm)	4,6±0,06	4,4±0,06**	4,79±0,13	4,1±0,09***	P<0,001
11	Pulmonary artery (mm)	22,6±0.03	21.6±0.03*	23,15±0.05	21,8±0.04*	P>0,05
12	Systolic pressure in the pulmonary artery (mm.Hg.col)	44.7±0.6	31.5±0.6***	43.2±0.6	34.2±0.6***	P<0,001
13	Left ventricular ejection fraction (%)	54.79±0.72	61.8±0.82** *	57.65±0.77	61.8±0.82	P<0,001

In this group, systolic, diastolic, and mean arterial blood pressure readings of both subgroups were reliably decreased ($P < 0.001$) after treatment. When the results were compared after treatments, it was found that the blood pressure in the first subgroup was reliably reduced ($P < 0.001$) compared to the second. This confirmed that bosentan had a higher peripheral blood pressure lowering effect than sildenafil.

In the first subgroup of patients receiving bosentan eplerenone, the left ventricle decreased reliably from 34.05 ± 0.56 to 32.1 ± 0.51 mm, ie 7.7% ($P < 0.05$), in the second subgroup receiving sildenafil eplerenone while decreased from 37.05 ± 0.54 to 32.1 ± 0.56 mm (1.09%), but the figures were unreliable ($P > 0.05$). The changes were also unreliable when comparing differences between the two subgroups after treatment. However, in the first small group receiving

bosentan eplerenone, the left ventricular values were confirmed to be more positive than in the second group (Table 4).

In the first subgroup, the values in the first subgroup decreased from 3.6 ± 0.06 mm to 3.3 ± 0.06 mm, respectively, and the difference between them was 8.3% ($P < 0.05$). In the second subgroup, it decreased from 3.5 ± 0.06 mm to 3.4 ± 0.06 mm, respectively, and the differences were 2.8% ($P > 0.05$). Postoperative changes were more pronounced in the group receiving bosentan eplerenone (2.8% vs. 8.3%).

Right ventricular size decreased by 3.7 ± 0.1 to 2.5 ± 0.06 mm before treatment in a small group receiving bosentan eplerenone based on standard treatment of COPD, the indicator was 32% reliable ($P < 0.05$), the second sildenafil eplerenone In the small group, the indicators decreased by 21% from 3.9 ± 0.04 to 3.08 ± 0.08 mm, respectively, and the differences were reliable. Comparing the



performance of the two subgroups after treatment, it was confirmed that the changes in the first group were 11% positive ($P < 0.001$) compared to the second subgroup.

Recent systolic volume readings in both subgroups increased from 41.0 ± 0.4 ml to 31.0 ± 0.4 ml, or 24%, and from 39.4 ± 1.05 ml to 32.4 ± 0.6 ml, respectively. that is, it decreased by 5.8%. In both subgroups, postoperative changes were significantly different from baseline ($P < 0.001$). However, it should be noted that in the first subgroup receiving bosentan eplerenone, the positive results were 18.2% higher than in the second subgroup.

The last diastolic volume was 90.9 ± 1.16 ml in the first subgroup receiving bosentan eplerenone. and 86.05 ± 1.26 ml. The positive shift was 5.3% and the indicator was reliable ($P < 0.05$). In the second subgroup, these values decreased from 92.85 ± 1.28 ml to 89.6 ± 1.2 ml, respectively, and the change was 2.18% ($P < 0.05$). Comparing the differences between the two subgroups after treatment, it was noted that the end-diastolic volume in the group receiving bosentan and eplerenone was reliably reduced compared to the group receiving sildenafil eplerenone ($P < 0.05$).

The last systolic measurements in both subgroups decreased from 3.01 ± 0.11 to 2.7 ± 0.11 cm (10.3%) in the first, respectively, and the reading was unreliable ($P > 0.05$). In the second subgroup, the values decreased from 2.93 ± 0.11 to 2.36 ± 0.14 cm, or 7.8%, respectively, and the changes were not reliable ($P > 0.05$). The differences between the groups after the treatments were 2.5% and no reliable change was observed ($P > 0.05$).

The last diastolic measurements in both subgroups decreased from 4.6 ± 0.06 to 4.4 ± 0.06 cm, respectively, in the first, and the reading was reliably 4.3% ($P < 0.001$). In the second subgroup, the values decreased from 4.79 ± 0.13 cm to 4.1 ± 0.09 cm, respectively, or by 12.7% ($P < 0.001$). The differences between the postoperative groups in the first were 8.4% higher than in the second, and a reliable change ($P < 0.05$) was noted.

In the first subgroup of patients in this group of patients with pulmonary artery diameter decreased from 22.6 ± 0.08 mm.sim.ust to 21.6 ± 0.03 mm.sim.ust (5.6%), the differences were reliable ($P < 0, 05$). In the second subgroup, the values decreased reliably ($P < 0.05$) from 23.15 ± 0.05 mm.sim.ust to 21.8 ± 0.04 mm.sim.ust (4.4%), respectively.

The systolic pressure in the pulmonary artery decreased reliably from 44.7 ± 0.6 mm.sim.ust to 31.5 ± 0.6 mm.sim.ust in the group receiving bosentan eplerenone ($P < 0.001$), which was 29.5%. In the second subgroup receiving sildenafil eplerenone, the values decreased from 43.2 ± 0.6 mm.sim.ust to 34.02 ± 0.6 mm.sim.ust, respectively, and the differences between pre- and post-treatment in this group were reliable ($P < 0.001$). Comparing the differences between the two groups after treatment, it was observed that the systolic pressure in the pulmonary artery was reliably ($P < 0.001$) lower than in the first, i.e., a small group receiving bosentan eplerenone.

Left ventricular hemorrhage fraction increased in the first subgroup by $54.79 \pm 0.72\%$ to $61.8 \pm 0.82\%$, and the differences were reliable ($P < 0.001$). In the second subgroup, no reliable ($P > 0.05$) change was observed in the hemorrhage fraction after treatment. In the first subgroup, the blood fraction fraction was found to be reliably increased ($P < 0.001$) relative to the second. This confirms that bosentan has a positive effect not only on the pressure in the pulmonary artery, but also on the left ventricular hemorrhage fraction.

Conclusion

In patients with chronic obstructive pulmonary disease with pulmonary hypertension, cardiac hemodynamic parameters change negatively in parallel with the severity of the disease.

In chronic obstructive pulmonary disease with pulmonary hypertension in stages II-III - IV of the disease with systolic pressure in the pulmonary artery right ventricle $r = 0.4$, $P < 0.01$; $r = 0.7$, $P < 0.01$; $r = 0.52$, between $P < 0.01$ and right subdivision size $r = 0.35$, P



<0.02; $r = 0.47$; $P < 0.002$ positive correlation was found. Positive correlations between pulmonary artery systolic pressure and end-diastolic and systolic volume ($r = 0.55$, $P < 0.001$ and $r = 0.39$, $P < 0.001$) in stage IV disease were observed not only in the right but also in the left side of the heart which confirms participation of the left ventricle of the heart. In addition, in the first subgroup of functional class IV of the disease, the increase in left ventricular systolic fraction by $54.79 \pm 0.72\%$ to $61.8 \pm 0.82\%$ and a reliable difference in the indicators from the second subgroup ($P < 0.001$) had a positive effect on bozentan. indicates that

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