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DINAMIC CHANGES BEFORE AND AFTER TREATMENT WHEN CHRONIC HEART FAILURE OCCURS IN VARIOUS COMORBIDITIES

Erkinova Nigora Erkinovna
Bukhara State Medical Institute

ABSTRACT	KEYWORDS
Experts of World Health Organization describe the growing prevalence of chronic diseases as a global epidemic of the XXI century. In recent years, special attention has been paid to diseases that are present in patients or occur on the basis of the underlying disease and are different from it.	

To define such cases, American epidemiologist researcher A.J. Feinstein recommended the term comorbid status of non-infectious diseases in 1970 [Naumova L.A., Osipova O.N. komorbidnost: mechanisms of pathogenesis, clinical knowledge // Modern problems of science and education. - 2016. - № 5]. Informations about the prevalence of comorbid conditions differ somewhat from each other, depending on a number of factors, including whether the patient is being treated in a primary care system or a specialized hospital, gender, age, tendency to medical examinations, and a number of other factors. But in all cases comorbidity increases with age of the patient [3 Atroshchenko E. S. Patient with chronic serdechnoynedostatochnostyu and soxranennoysystolicheskoyfunktsieylevogojeludochka / E. S. Atroshchenko // Serdechnayanedostatochnost. - 2007. - T. 8, № 6. - p. 297-300; 33EwansW. E. Pharmacogenomics - DrugDisposition, DrugTargets, andSideEffects / W. E. Ewans, H. L. McLeod // N. Eng. J. Med. - Vol. 3. - 2003. - Feb. - Vol. 48, N 6. - R. 538-549]. The incidence of the phenomenon of comorbidity increases to 69% at the age of 18-44 years, 93% at the age of 45-64 years, and 98% at the age of 65 years [23Sychev D. A. Clinical pharmacogenetics of R-adrenoblockers / D. A. Sychev, G. V. Ramenskaya, I. V. Ignatev [i dr.] // Klin. medical. - 2006. - № 3. - p. 20-26; 28CIBISInvestigatorsandCommittees. A randomized trial of beta-blockade in heart failure. - Circulation. - 1994. - Vol. 90. - P. 1765-1773 .; 33]. Almost all studies have shown that a high level of comorbidity leads to a decrease in the quality of life, disruption of social harmony and an increase in mortality [11. Description of barriers to self-care by persons with comorbid chronic diseases / E. A. Bayliss [et al.] // Annals of Family Medicine. - 2003. -Vol. 1, № 1. - P. 15-21.12. Dickson V. V. A qualitative meta-analysis of heart failure self-care practices among individuals with multiple comorbid conditions / V. V. Dickson, H. Buck, B. Riegel // J. of Cardiac Failure. - 2011. -Vol. 17, № 5. - P. 413-419. 17] 21.12. Dickson V. V. A qualitative meta-analysis of heart failure self-care practices among individuals with multiple comorbid conditions / V. V. Dickson, H. Buck, B. Riegel // J. of Cardiac

Failure. - 2011. -Vol. 17, № 5. - P. 413-419. 17].The prevalence and growing number of comorbidities underscores the importance of studying this issue for many countries, including Uzbekistan. [11. Belyalov F. I. Treatment of internal diseases in the conditions of comorbidity: monogr. / F. I. Belyalov. - 8-e izd. - Irkutsk: RIO IGIUVa, 2012. -285 p, 88. A systematic review of prevalence studies on multimorbidity: Toward a more uniform methodology / M. Fortin [et al.] // Annals of Family Medicine. -2012. - Vol. 10, № 2. - P. 142-151.].

It is known that one of the main causes of fatalty is cardiovascular diseases and in some cases it is complicated by chronic heart failure (CHF)(Jhund P.S., Macintyre K., 2009; BelenkovYu.N., MareevV.Yu., 2011).

In European countries, the prevalence of CHF is 2.1%, 90% of women and 75% of men over the age of 70. In the United States, these numbers range from 1–1.5% and appear in 10% of the population over age of 60 [99. Gurevich M. A. Nekotoryeosobennostiklinikivalecheniyaxronicheskoyserdechnoynedostatochnosti u pojilyh / M. A. Gurevich // Ross. cartiol. jurn. - 2002. - T.33, № 1. - P. 81-84., 19. Provotorov V. M. Diagnostika xronicheskoy serdechnoy nedostatochnosti narannixstadiyax u litspojilogovozrasta / V. M. Provotorov, E. S. Burlova // Klin. gerontology. - 2007. - T. 13, № 6. - P. 57-62].

According to data from a number of leading researchers around the world, the joint of neighbor diseases to CHF, not only has worsened the general consequence , but also increases the number and duration of hospital treatments **[14Lang C. C. Cardiacomorbiditis.Christianart.Ch. - 2007. - vol. 93. - P. 665-671., 16. Thirty-day re-hospitalization after acute myocardial infarction: a cohort study / S. M. Dunlay [et al.] // Chronicles of Internal Medicine. - 2012. -Vol. 157, № 1. - P. 11-18],**and that is considered to be the main cause of death. Some authors compare the dynamics of observations of the fatality in the CHF with the fatality of the causes of oncological diseases **[1. AGeev F. T. Is it necessary to follow the recommendations for the treatment of cardiac insufficiency, based on the results of international clinical research? Znachenie isvedovaniya SENIORS dlya rossiyskoy populyatsii bolnyx XSN / F. T. Ageyev // Serdechnayanedostatochnost. - 2006. - T. 6, № 6. - P. 258-262., 10 Izbrannyeletsii po kardiologii / Pod red. E. V. Shlyxto. - SPb. : Petersburg; Ladoga, 2006. - P. 8-14].**Observations showed that the incidence of comorbidities is sometimes as high as 90%. Among them diabetes mellitus (DM), coronary heart disease (CHD), arterial hypertension (AH), obesity, anemia, and hyperlipidemia are more occured**[99. Gurevich M. A. Nekotorye osobennosti kliniki vale cheniyaxronicheskoy serdechnoynedostatochnosti u pojilyh / M. A. Gurevich // Ross. cartiol. jurn. - 2002. - T.33, № 1. - P. 81-84., 19. Provotorov V. M. Diagnostika xronicheskoy serdechnoy nedostatochnosti na rannix stadiyax u litspojilogovozrasta / V. M. Provotorov, E. S. Burlova // Klin. gerontology. - 2007. - T. 13, № 6. - P. 57-62] .33EvansW. E. Pharmacogenomics - Drug Disposition, DrugTargets, and SideEffects / W. E. Evans, H. L. McLeod // N. Eng. J. Med. - Volume 3. - 2003. - February - Vol. 48, N 6. - R. 538-549.].**

According to facts of R.T Shukurov and T.A Abdullayev, in most cases in the Republic the etiological cause of CHF (58.8%) is IHD, and it is often combined with (68.3%) AH. There is blood in the left ventricleIn a study of patients with different driving fractions, systolic and diastolic dysfunction were found in more men, overweight in the low driving fraction (41.1%) and obesity in the preserved group (51.6%). The main causes of myocardial injury in patients with low left ventricular blood flow fraction were myocardial infarction (91.1%), co-occurrence of IHD with AH (81.3%), obesity (51.6%) and DM

(43.8%). Chronic obstructive pulmonary disease in 26.8% of cases of extracardiac comorbidities in this group of patients, obleterative atherosclerosis of the arteries of the legs in 17.9%, pneumonia in patients with driving fraction and varicose veins of the legs in 34.4%. detected**(Р.Т. ШукуровиТ.А. Абдуллаев, Гендерные различия и коморбитность у больных с ХСН. Кардиоваскул. Терапия и профилактика 2017, 16(6) с.87-91).**

According to L.GStrongin's observations, more chronic kidney disease (CKD) occurs in the comorbid structure of CHF. It was found that the combination of these two complications increased the average number of hospitalizations for all causes by 1.30 ± 0.44 and 1.05 ± 0.32 r = 0.01, respectively, in patients with heart failure alone, and the average number of treatments per year duration is 15.2 ± 3.9 and 17.3 (R> 0.001), respectively, thus significantly increasing its cost **[66. Серов В. А. Эпидемиология хронической болезни почек у больных с хронической сердечной недостаточностью / В. А. Серов, А. М. Шутов, М. В. МеНЗороВ // Неврология. - 2010. -Т. 14, № 1. - С. 50-55]** .Hence, the functional status of the kidneys has a very negative effect on the course and outcome of CHF.**(6Klausen K., Scharling H., Jensen J. Very low level of microalbuminuria is associated with increased risk of death in subjects with cardiovascular or cerebrovascular diseases // Intern. Med. — 2006; 260 (3): 231–237).** At present, in many studies, the detection of renal dysfunction is based on the amount of creatinine in the serum, the rate of glomerular filtration rate (RGF) and oralbuminuria [4,54. **Резник Е.В., Гендлин Г.Е., Сторожаков Г.И. и др. Изменения функции почек у больных ХСН // Сердечная недостаточность 2007; 8(2): 89-94.5. Резник Е.В., Гендлин Г.Е., Сторожаков Г.И. и др. Почечнаягемодинамикаубольныххроническойсердечнойнедостаточностью // Сердечнаянедостаточность 2007; 8(3): 118-123.]**

Albuminuria is one of the early signs of kidney damage, reflects the early stages of vascular changes (endothelial dysfunction, atherosclerosis) and increases mortality not only from kidney but also from cardiovascular disease. Increased albuminuria has a negative effect on vascular condition **(4Karalliedde J., Viberti G. Microalbuminuriaandcardiovascularrisk. Am J Hypertens 2004; 17: 986–93).**

Although there are no clear data confirming the pathophysiological mechanisms of protein excretion in the urine, it is thought that it is caused by vascular dysfunction, systemic inflammation, neurohumoral activation. **(European Journal of Heart Failure (2011) 13, 746–754doi:10.1093/eurjhf/hfr031. Associations of albuminuria in patients withchronic heart failure: findings in the ALiskirenObservation of heart Failure Treatment studyColette E. Jackson1, Michael R. MacDonald1, Mark C. Petrie1, Scott D. Solomon,Bertram Pitt, Roberto Latini, Aldo P. Maggioni, Beverly A. Smith,Margaret F. Prescott, Jim Lewsey, John J.V. McMurray, for the ALiskirenObservation of heart Failure Treatment (ALOFT) investigators.; Deckert T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen T, Kofoed-EnevoldsenA.Albuminuria reflects widespread vascular damage. The Steno hypothesis.Diabetologia1989; 32:219–226; Silverberg D, Wexler D, Blum M, Schwartz D, Iaina A. The association betweencongestive heart failure and chronic renal disease.CurrOpinNephrolHypertens2004;13:163–170).** Among them, the activation of the renin-angiotensin-aldosterone system plays an important role in the manifestation of cause and effect, which is emphasized by some researchers. Micro-albuminuria is an increase in the loss of albumin from the blood plasma through the endothelium and is a marker of the development of systemic endothelial dysfunction. This is typical for the early stages of atherosclerosis and is also

directly related to the increased risk of cardiovascular disease and death from them. [**3,4Gerstein H. C., Mann J. F., Yi Q. etal. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA, 2001; 286: 421–6. 4. Karalliedde J., Viberti G. Microalbuminuria and cardiovascular risk. Am J Hypertens 2004; 17: 986–93].**In one of the LIFE sub-studies **[10WachtellK.,IbsenH., OlsenM. H. etal. Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy: the LIFE study. AnnInternMed, 2003; 139: 901–6]** confirmed that increased urinary protein excretion is important in the development of left ventricular hypertrophy, regardless of the patient's age, sex, race, blood pressure level, presence of DM, smoking, and creatinine level in the blood. According to the data, micro-albuminuria is observed in 15-40% of patients with type 2 DM. **[4,7Pedrinelli R., Dell'Omo G., DiBello V. etal. Microalbuminuria, an integrated marker of cardiovascular risk in essential hypertension. J Hum Hypertens, 2002; 16: 79–89.9Volpe M. Microalbuminuria screening in patients with hypertension: Recommendations for clinical practice. Int J ClinPract 2008, 62 (1): 97–108.)]**In one of the meta-analyzes, 26 cohort studies examined the correlation between micro-albuminuria and cardiovascular disease in 170,000 patients. It was found that the risk of developing cardiovascular disease was higher than 50% in patients who did not have it. Numerous experimental, clinical, and epidemiological studies have shown that micro-albuminuria is one of the important risk factors for cardiovascular and cerebrovascular conditions. [**5KlausenK, JohnsenKB, RasmussenFetal. Very low levels of microalbuminuria are associated with an increased risk of coronary heart disease and death independent of renal function, hypertension, and diabetes. AmHeartAssociation 2004; 110:32–35].**

In addition, micro-albuminuria is assessed as an early marker of renal and glomerular damage and endothelial dysfunction. As the functional class of CHF increases, the degree of proteinuria increases too. Many researchers have linked micro-albuminuria to impaired ball filtration function and increased intracranial pressure.[**44. РезникЕ.В., ГендлинГ.Е., СторожаковГ.И. идр. Изменения функции почек у больных ХСН // Сердечная недостаточность 2007; 8(2): 89-94.,99. DamsgaardEM, FrolandA, JorgensenODetal. Microalbuminuriaaspredictorofincreasedmortalityinelderlypeople // BMJ 1990; 300: 297].** Data from the cited literature confirm that one of the most common syndromes in CHF is albuminuria, in which a high protein content in the urine indicates the severity of the disease.**[74[73, 73. Моисеев, В.С. Болезни сердца / В.С. Моисеев, А.В. Сумароков. - М.: Универсум Паблишинг, 2001. - 256 с.7474. Моисеев, В.С. Нефрологические аспекты застойной сердечной недостаточности / В.С. Моисеев, В.В. Фомин // Тер. арх. - 2003. - № 6. - С. 84-89.].**

Systemic oxidative stress, serum tumor necrosis factor, and high levels of other inflammatory cytokines play a leading role in the development of glomerular capillary endothelial dysfunction. This, in turn, leads to the loss of negative charges in the endothelium of the glomerular filter capillaries and an increase in its permeability. **[205205. Futracul, N. Microalbuminuria - a biomarker of renal microvascular disease / N. Futracul, V. Sridama, P. Futracul // Ren. Fail. - 2009. - Vol. 31, № 2. - P. 140-143**]. However, in the available literature, more attention has been paid to the degree of albuminuria and the functional state of the heart and kidneys in patients with CHF type II QD. But as mentioned above, CHF is often accompanied by several comorbid diseases. Logically, their abundance leads to not only functional but also fibrous changes in the heart and kidneys.The occurrence of these changes is manifested by proteinuria, which has a mutually reinforcing effect on each other. In this

context, the study of the relationship between albuminuria and fibrosis markers in CHF with varying degrees of comorbid diseases and the assessment of the effect of complex pathogenetic therapies on them is important for practical medicine.

MATERIALS AND METHODS

The 120 patients with CHF in our follow-up were divided into three groups, with the first group consisting of 40 patients with CHF II-III FC albuminuria and one comorbid disease. Their mean age was 58.3 ± 4.2, 17 were male and 23 were female. The second group consisted of 40 patients with CHF II-III FC albuminuria and two comorbid diseases, with an average age of 61.8 ± 4.7, 19 men and 21 women.

The third group also consisted of 40 patients with CHF II-III F C albuminuria diagnosed and three or more comorbidities. Their mean age was 65.9 ± 5.3, of which 21 were male and 19 were female. In all cases, it was found that CHF was caused by UIC, post-infarction cardio-sclerosis and hypertension. In some cases, it was noted in the anamnesis and objective examination that IHD and AG caused CHF in one patient at the same time. All patients received 25-50 mg of eplerenone, the latest generation of mineralocorticoid receptor antagonist as a standard treatment of CHF, b-blockers, alsisartan as an angiotensin II receptor antagonist, and anti-fibrotic agent. Based on the instructions, cardiac glycosides, diuretics and antiarrhythmic drugs were prescribed in individual cases. Potassium levels and glomerular filtration rate (> 60 ml per 1.72 m2 body level) were monitored in all patients in the follow-up. Eplerenonewas discontinued in cases of hyperkalemia.

Data on comorbidities identified in the patients in our follow-up are presented in Table 1.

Table 1 INFORMATION ON COMOMBIDE DISEASES DETECTED IN PATIENTS RESEARCHED FOR RESEARCH

№	**Groups** / **Indicators**	**Patients with chronic heart failure II-III FC with albuminuria and a single comorbid disease n = 40**		**Patients with chronic heart failure II-III FC with albuminuria and two comorbidities n = 40**		**Patients with chronic heart failure II-III FC albuminuria and three or more comorbid diseases n = 40**	
		Absolute	%	Absolute	%	Absolute	%
1	Men	17	42,5	19	47,5	21	52,5
2	Women	23	57,5	21	52,5	19	47,5
3	Middle age	58,3±4,2		61,8±4,7		65,9±5,3	
DISEASES CAUSED BY HEART FAILURE							
1	Ischemicheartdisease	18	45	20	50	22	55
2	Ischemic heart disease, post-infarction cardiosclerosis	12	30	15	37,5	17	42,5
3	Hypertension	10	25	8	20	7	17,5
COMORBIDE DISEASES							
1	Obesity	7	17,5	8	20	8	20

2	Diabetesmellitus II	5	12,5	6	15	7	17,5
3	Chronicpyelonephritis	7	17,5	8	20	20	50
4	Chronicgastritis	5	12,5	15	37,5	14	35
5	IntestinalSyndrome	4	10	13	32,5	20	50
6	Period of remission of chronic bronchitis	2	5	4	10	20	50
7	Remission period of chronic obstructive pulmonary disease	1	2,5	7	17,5	17	42,5
8	Good quality adenoma of the prostate gland	2	5	6	15	14	35
9	Anemia 1, 2 degrees	5	12,5	10	25	17	42,5
10	Chronichepatitis	2	5	3	7,5	4	10

In order to study the relationship between albuminuria and fibrosis markers and their preoperative and postoperative dynamics, cystatin-S, aldosterone, b1-transforming growth factor (TGF-b1) levels in the blood were determined using the enzyme-linked immune-sorbent method. So, patients 'endurance to physical exertion was also assessed in meters, quality of life, and clinical status in points (Table 2).

Table 2 Some biochemical parameters and physical and clinical condition of patients, when chronic heart failure occurs with a variety of comorbid diseases

№	**Groups** / **Indicators**	**Patients with chronic heart failure II-III FC with albuminuria and a single comorbid disease n = 40**	**Patients with chronic heart failure II-III FC with albuminuria and two comorbidities n = 40**	**Patients with chronic heart failure II-III FC albuminuria and three or more comorbid diseases n = 40**
1	The amount of protein lost overnight (mg / l)	335,6 ± 15,3	499,9 ± 18,9	614,4 ± 23,3
2	Cystatin-S (mg / l)	1,36 ± 0,05	1,53 ± 0,03	1,65 ± 0,04
3	Aldosterone (PG / ml)	563,1 ± 28,3	699,2 ± 31,2	708,5 ± 45,7
4	b1-transforming growth factor (pg / ml)	2390,8 ± 98,3	2466,2 ± 150,4	2735,8 ± 190,2
5	Six-minute walking test (meters)	391,1 ± 11,0	335,5 ± 8,0	259,1 ± 9,8
6	Qualityoflife (points)	48,9 ± 2,1	55,6 ± 1,9	58,3 ± 2,0
7	Clinicalstatus (points)	5,4 ± 0,19	6,1 ± 0,4	6,88 ± 0,17

RESULTS OF RESEARCH

The correlation between the level of albuminuria and fibrosis markers aldosterone, TGF-b1 as well as their resistance to physical loads (six-minute walking test) in clinical patients and quality of life was studied in 120 patients with CHF in our follow-up.

CORRELATION BETWEEN ALBUMINURIA, FIBROZE MARKERS AND GENERAL SITUATION OF PATIENTS , WHEN CHRONIC HEART FAILURE OCCURS WITH VARIOUS COMORBIDE DISEASES.

It is known that aldosterone is involved in water-salt metabolism, causing a number of changes in its amount in the blood. In the CHFincrease in this hormone in the blood is caused not only by the activation of the renin-angiotensin system, but also by a decrease in its clearance due to changes in the liver. As a result, the half-life period of aldosterone in plasma is significantly increased, and the amount of the hormone in the serum increases by 3-4 times. According to recent data, aldosterone not only affects water-salt metabolism, but also leads to the development of fibrosis processes in CHF. In this context, the inhibition of aldosterone production by slows the development of fibrous processes of CHF. Therefore, the study of the interaction of aldosterone with albuminuria in different comorbid conditions of CHF is of some practical importance (Figure 1).

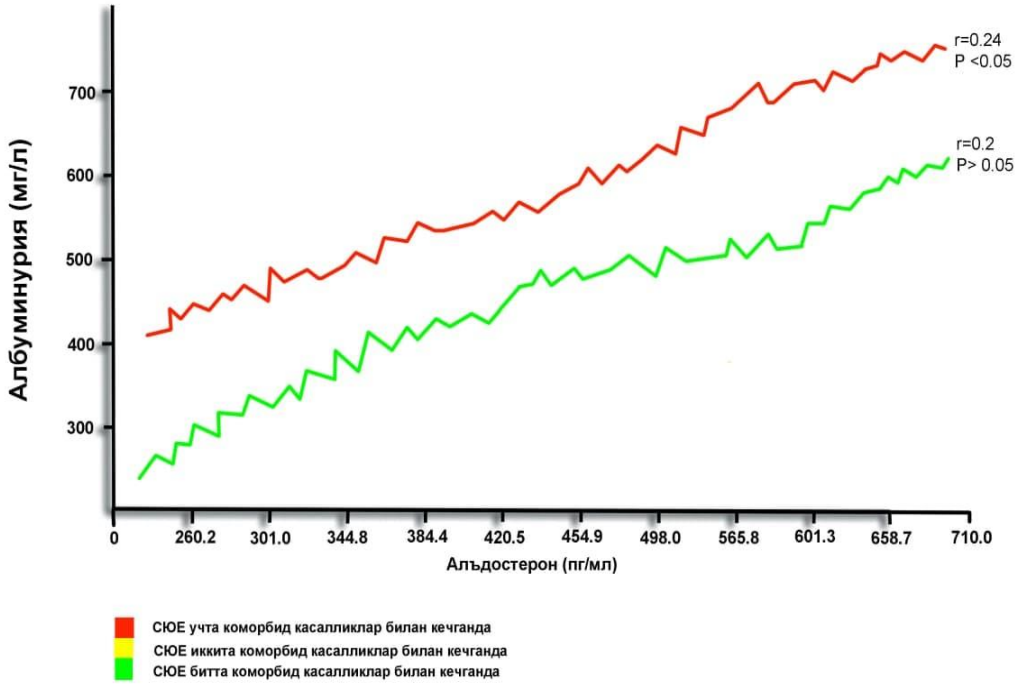

Figure 1. Correlation between albuminuria and aldosterone in chronic heart failure with a number of comorbid diseases

A reliable correlation between albuminuria and aldosterone was found in the second and third groups of patients (r = 0.2; R <0.058 and r = 0.24; P <0.05), as shown in the diagram, in the case of CHF with one, two and three or more comorbid diseases. Thus, the development of fibrous processes in the patient's body and, above all, in the heart and kidneys, in parallel with CHF in parallel cases is accompanied by albuminuria. TGF-b1 belongs to the family of classic cytokines and is a leading factor in the proliferative chain not only in the development of heart and blood vessels , but also

nephrosclerosis. An increase in its amount in the blood of patients with CHF reflects the interdependence of fibroplastic changes. Uremic toxins produced in the proximal segments of the nephron increase the concentration of TGF-b1 in the blood. It, in turn, accelerates the process of tubule-interstitial fibrosis, which is the main cause of loss of renal function. In this context, it is important to study the relationship between albuminuria and this cytokine (Figure 2).

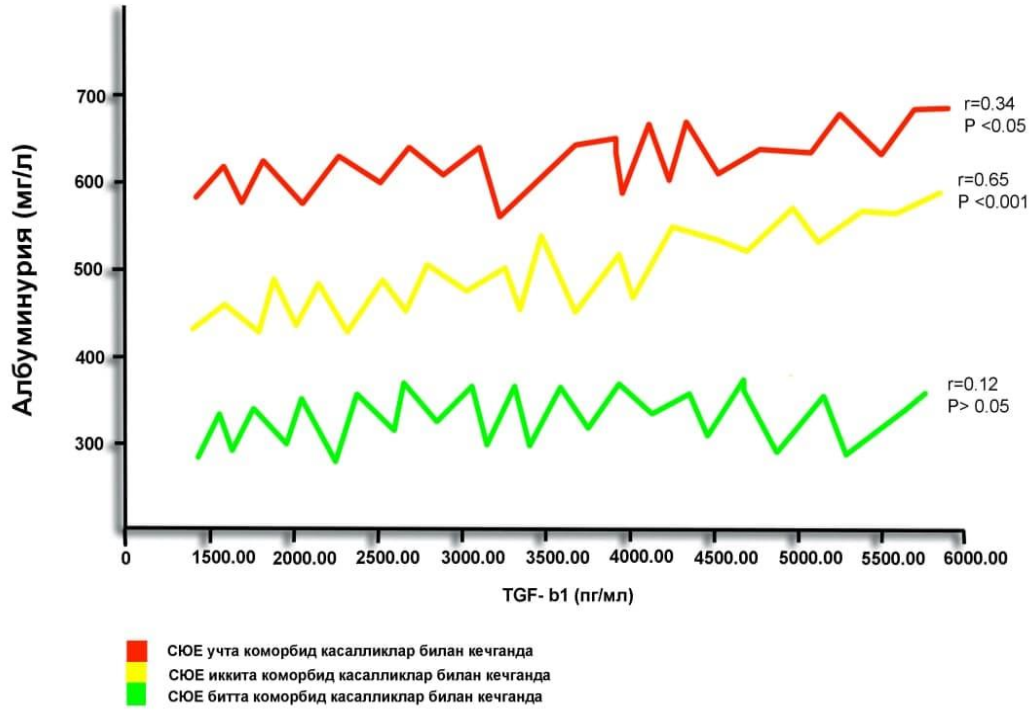

Figure 2. Correlation between albuminuria and TGF-b1 in chronic heart failure with a number of comorbid diseases

In this case, CHF between albuminuria and TGF-b1 in one comorbid disease r = 0.12 (R> 0.05), in two and three or more comorbid diseases r = 0.65 (P <0.001) and r = 0 , 34 R <0.05) correlation was determined. This confirms that albuminuria is a marker indicating not only the functional status of the kidney but also the processes of tubulointerstitial fibrosis in it.

The main effectiveness of treatment of patients in accordance with generally accepted principles is determined by the improvement of their quality of life and prolongation of life. In this context, it is of practical importance to study the effects of albuminuria on patients' physical endurance, clinical condition, and quality of life when CHF occurs with a variety of comorbid conditions. The correlation between albuminuria and the six-minute gait test was r = 0.1 (R> 0.05) when CHF was present with a single comorbid disease. With two and three or more comorbid diseases, r = 0.19 (R <0.001) and r = 0.12 (R <0.05), respectively, changed reliably (Figure 3).

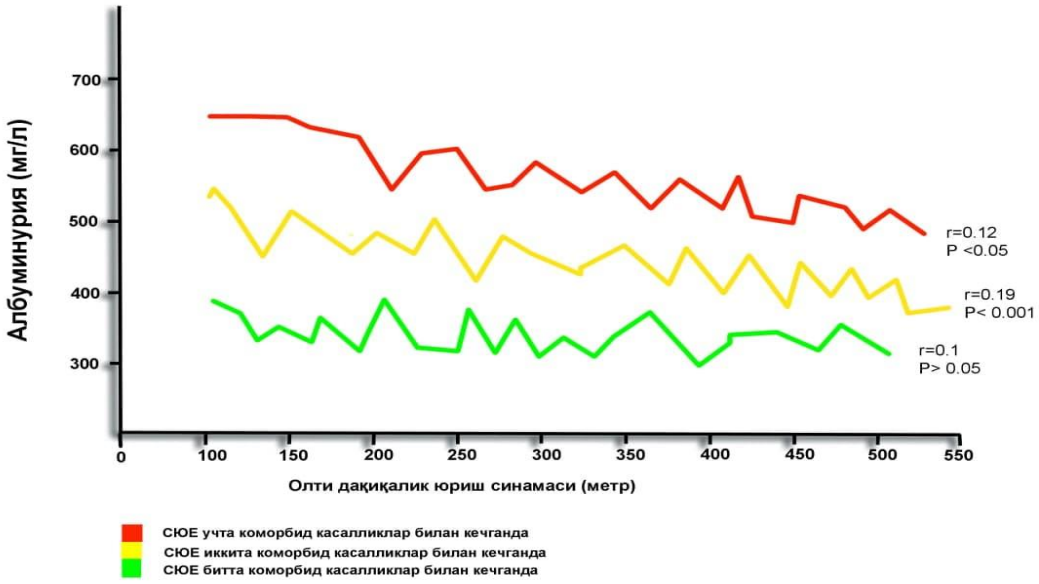

Figure 3. Correlation between albuminuria and six-minute walking test in chronic heart failure with a number of different comorbidities

That is, it was found that an increase in the inclusion of CHF comorbid diseases led to a decrease in patients 'resistance to physical exertion. The correlation between albuminuria and their clinical status in patients, when CHF occurs with various comorbid diseases was studied, the following was found (Figure 4).

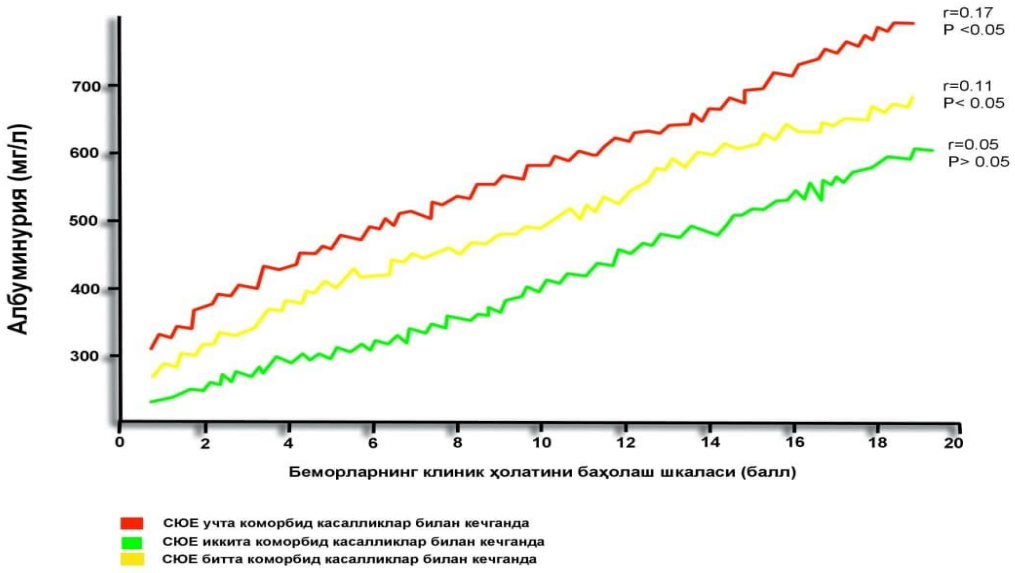

Figure 4. Correlation between albuminuria and clinical status scores when chronic heart failure is associated with a different number of comorbidities.

CHF with one comorbid disease r = 0.05 (P> 0.05), with two comorbid diseases r = 0.11 (P <0.05) and with three or more comorbid cases r = 0.17 (P < 0.05) and the clinical condition of the patients in the last two groups was markedly worsened.

We also examined the correlation between albuminuria and quality of life in the patients we observed (Figure 5).

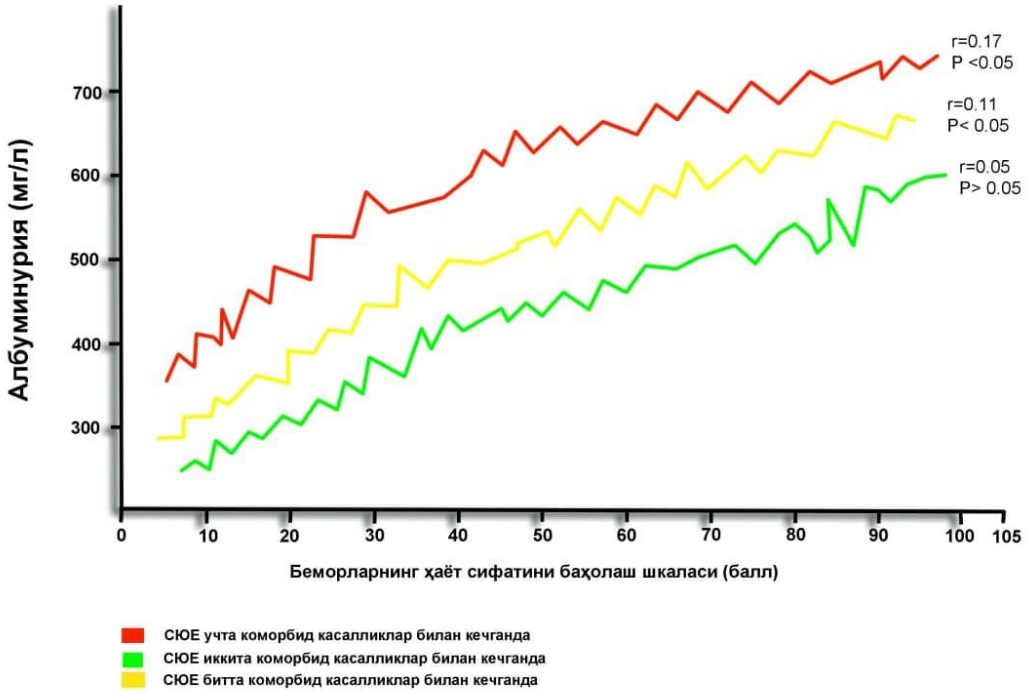

Figure 5. Correlation between albuminuria and quality of life scale in chronic heart failure with a different number of comorbid diseases

Then CHF with one comorbid disease r = 0.05 (P> 0.05) , r = 0.11 (P <0.05) and r = 0.17(P<0.05) in two and three comorbid diseases, respectively were found.

These findings confirm that patients' resilience to physical exertion, clinical condition, and quality of life deteriorated reliably when their number was two or more and when they underwent various comorbid conditions.

THE INDICATORS OF ALBUMINURIA, ALDOSTERONE, AND TGF-b1, WHEN CHRONIC HEART FAILURE OCCURS WITH VARIOUS COMORBIDE DISEASES, BEFORE AND AFTER TREATMENT.

In the next step, we studied albuminuria, aldosterone, and TGF-b1 levels before and after CHF standard treatment in 25 patients from each group.

In this case, as mentioned above, the last representative of the angiotensin II receptor blocker azilsartan, medoximil and mineralocorticoid receptor antagonist eplerenone were used. Its antifibrotic effect was taken into account when prescribing the last drug. The change of albuminuria in various comorbid cases after complex treatments performed in CHF is shown in Figure 6.

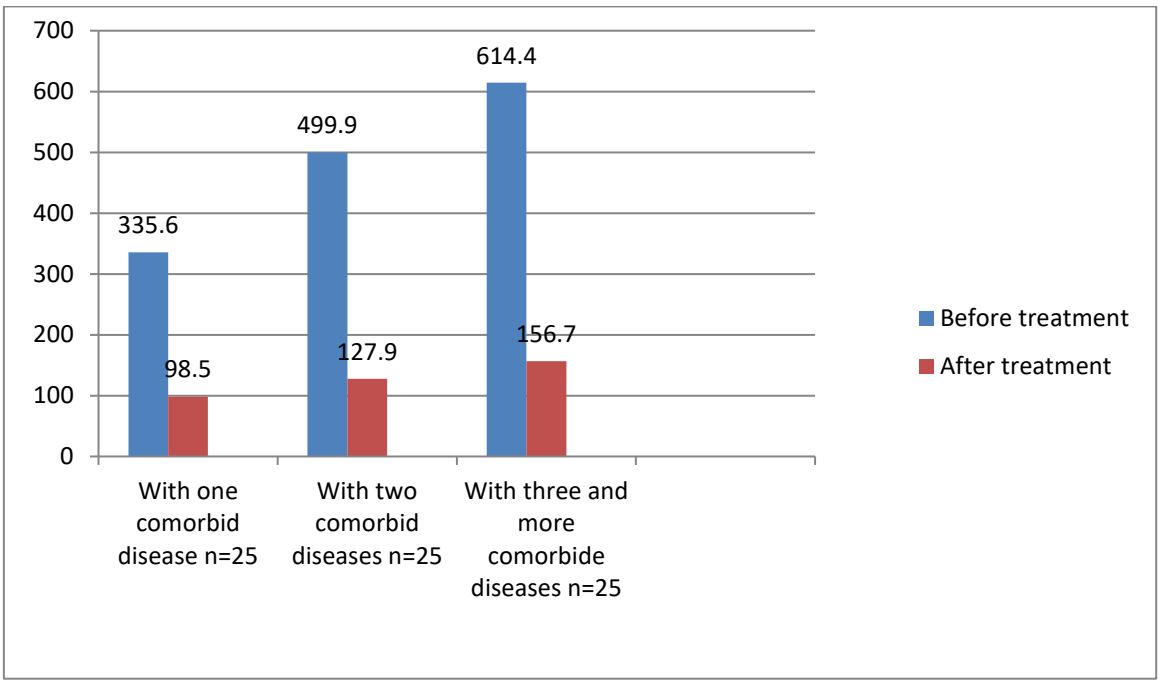

Figure 6. Before and after treatment of chronic heart failure with a number of comorbid diseases, albuminuria (mg / l)

In patients with CHF with a single comorbid disease, nocturnal proteinuria decreased from 336.6 ± 15.3mg / l to 98.5 ± 8.7mg / l i.e. 3.4-fold (P <0.001) after three months of complex treatments, that was 499.9 ± 18.9 mg / l and 127.9 ± 9.7 mg / l, or 3.9 times (P <0.01), 614.4 ± 23, respectively, in patients with three or more comorbid diseases, it decreased from 3 mg / l to 156.7 mg / l i.e. 3.9 times (P <0.001). These figures confirm that the level of albuminuria in patients with CHF is directly related to comorbid diseases, with an increase in protein excretion in the urine in parallel with an increase in their number. Complex standard treatments have a positive effect on the process, leading to a reliable reduction in proteinuria.

It is known that the CHF plays a key role in development of fibrous processes in the heart and kidneys, one of the leading factors in the rapid development of the disease, the transition to severe stages and the death of patients. In this context, we studied the effect of fibrosis markers on aldosterone and TGF-b1 when the standard treatment containing azilsartan and eplerenonewas used in when CHF occurs with various comorbid conditions.

CHF with a single comorbid disease increased from 563.1 ± 28.3 pg / ml to 247.4 ± 13.4 pg / ml before and three months after aldosterone treatment, that is 2.27 times, with two and three or more comorbid diseases that decreased from 699.2 ± 31.2 pg / ml to 402.2 ± 23.4 pg / ml and from 708.5 ± 45.7 to 415.1 ± 29.4 pg / ml, or 0.7 times, respectively.(Figure 7).

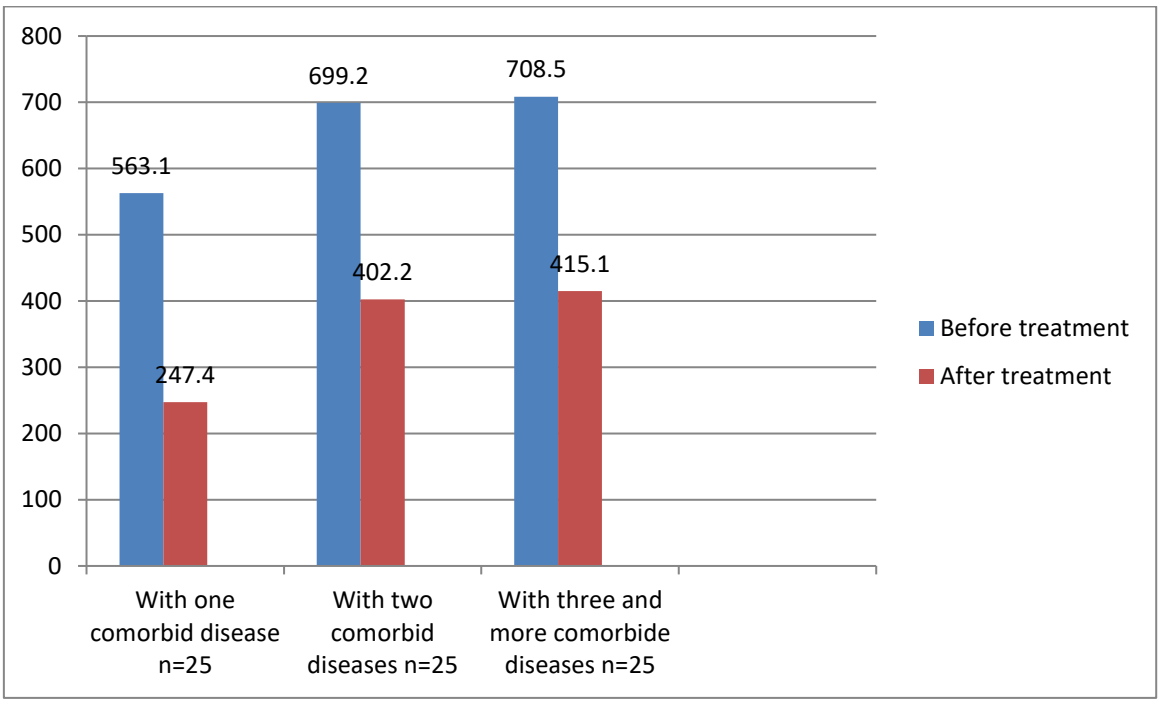

Figure 7. Aldosterone levels before and after treatment in chronic heart failure with a number of comorbidities (pg / ml)

In all cases, a reliable decrease in serum aldosterone was observed after treatment. At the same time, as mentioned above, this decrease rate (2.27; 1.74; and 0.7) is inextricably linked with the number of comorbid diseases, and as they increase, a decrease in positive shifts is also observed.

Pre- and post-treatment levels of TGF-11 in the follow-up patients also varied in proportion to the number of comorbidities. In one comorbid disease from 2390.8 ± 98.3 pg / ml to 1092.9 ± 78.4 pg / ml, (P <0.001) in two and three or more comorbid diseases, respectively 2466.2 ± 150.4 pg / ml ml decreased to 1859.8 ± 103 pg / ml and from 2735.8 ± 190.2 to 2187.6 ± 150.3 pg / ml reliably (P <0.001) (Figure 8).

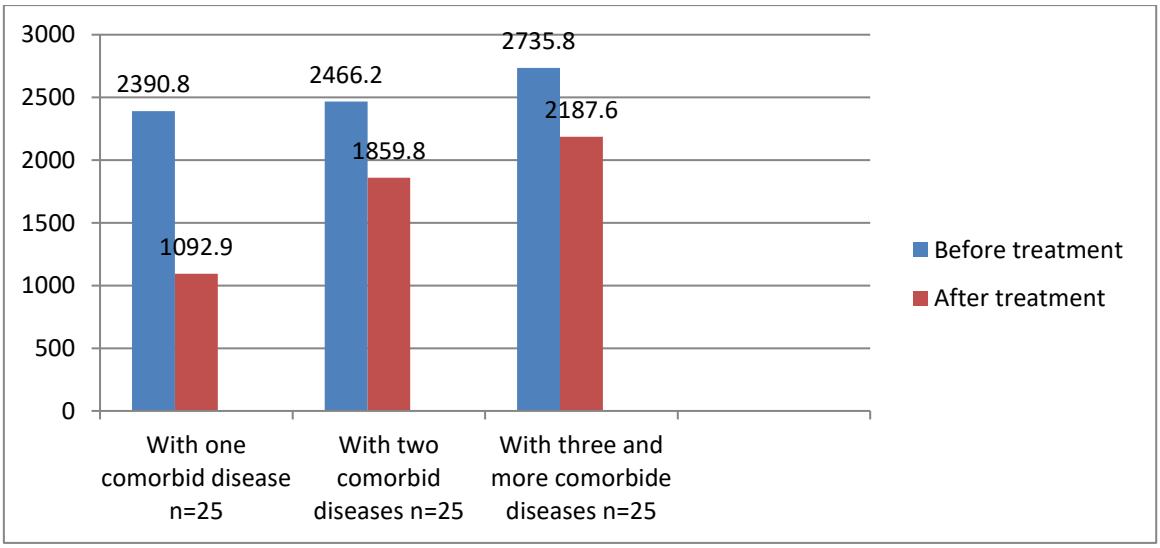

Figure 8. TGF-b1 levels before and after treatment in chronic heart failure with a number of comorbidities (pg / ml)

When CHF was associated with one or two and three or more comorbid diseases, TGF-b1 values decreased 2.18, 1.32, and 1.25 times, respectively, after treatments. At the same time, in cases where one comorbid condition was detected, a reliable decrease in TGF-b1 was achieved compared to the other two groups.

Thus, the complex treatments performed resulted in a reliable reduction of fibrosis markers and therefore stabilization of the process. But positive changes are more pronounced when CHF passes with a single comorbid disease.

SIX-MINUTE WALKING TEST, SCALE OF ASSESMENT CLINICAL SITUATION, INDICATORS OF MINNESOT QUESTIONAIRESURVEY BEFORE AND AFTER TREATMENT OF CHARACTERISTIC HEART FAILURE IN DIFFERENT NUMBER OF COMORBIDE DISEASES.

The six-minute walking test, the clinical condition assessment scale, and the Minnesota questionnaire are widely used in scientific and practical medicine to evaluate the creative outcomes achieved in the treatment of CHF. In this context, we studied their performance before and after treatments, taking into account the number of comorbidities in the patients in our follow-up.

In patients with single, double, and triple or more comorbidities, the six-minute walking test values before and after treatment ranged from 391.1 ± 11.0 to 469.03 m and from 335.5 ± 8.0 to 423 ± 9, respectively and positively changed from 259.1 ± 9.8 to 276.7 ± 12.3 m, and in all cases P <0.001 (Figure 9).

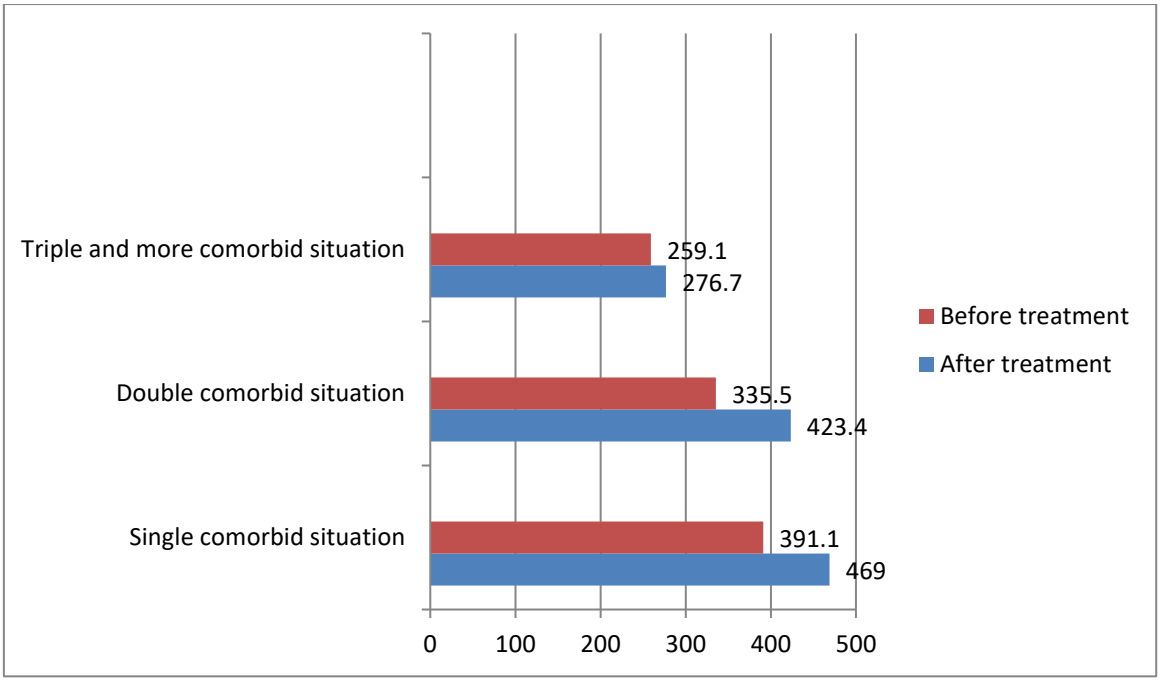

Figure 9. Indications for 6-minute walking test before and after treatment of chronic heart failure in various comorbid conditions

It was noted that in the first group the figure increased by 78 meters, in the second group by 88 meters and in the third group by 12.9 meters.

When assessing quality of life in the Minnesota questionnaire, before and after treatment, the scores were 48.9 ± 2.1 points and 25.5 ± 1.77 (P <0.001) or 23.4 points, respectively, 55.6 ± 1.9 and 28,

improved by ± 2.8 (P <0.001) or 27.1 points, 58.3 ± 2.0, 34.0 ± 7.0 (P <0.001), or 24.3 points (Figure 10).

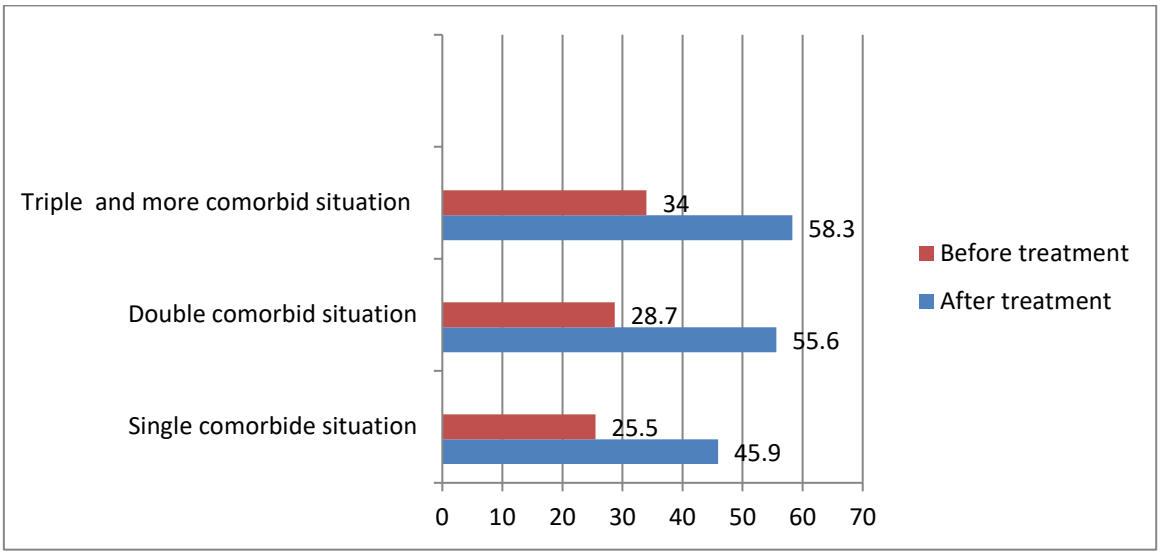

Figure 10. Indicators of quality of life scores before and after treatment when chronic heart failure occurs in various comorbid conditions

The analysis confirms that the quality of life of all patients changed reliably after three months of treatment in all groups of patients.

Also, in the clinical status assessment scale before and after CHF treatment, the scores improved from 20.4 to 5.4 ± 0.19 to 3.4 ± 0.23, in a single comorbid disease, and improved to 20, in two comorbid cases scores from 4 to 4.38 ± 0.13 decreased to 1.74, and in patients with three or more comorbidities decreased from 6.88 ± 0.17 to 4.56 ± 0.2, respectively and scores changed 2.32 indicator to the positive side. (Figure 11).

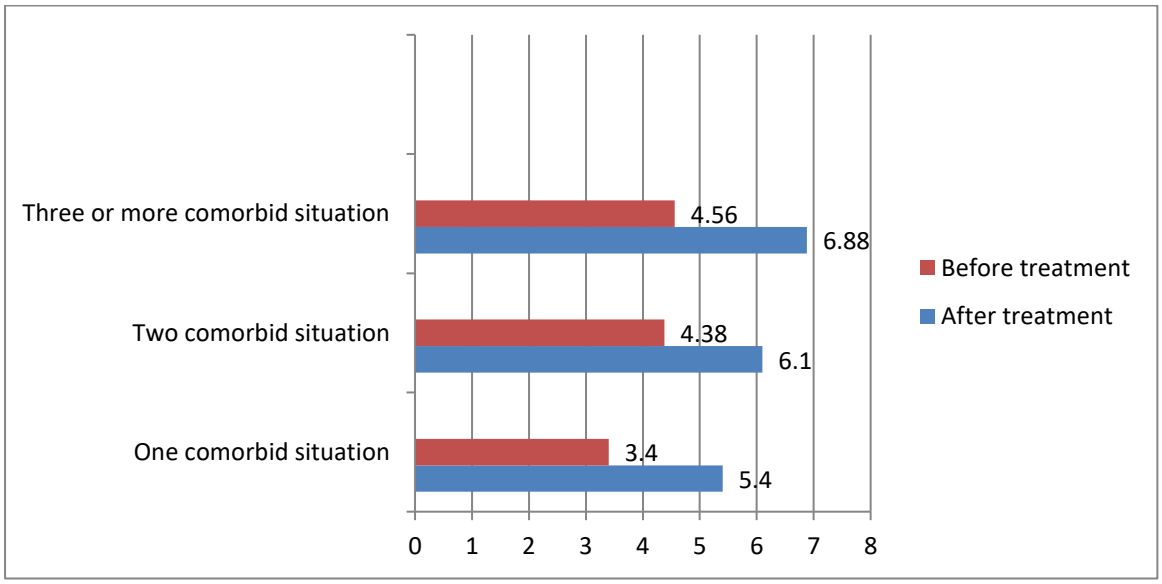

Figure 11. Indicators of clinical status scores before and after treatment in chronic heart failure with various comorbid conditions.

The figures show that the analyzes had a reliable (P<0.05) positive effect on the clinical condition of the patients.

After the following treatments, confirmed that the endurance to physical quality, and clinical condition of the existing in patients with CHF had changed for the better in proportion to the number of comorbid cases.

CONCLUSIONS

1. As the number of CHF comorbidities increases, so does the rate of overnight proteinuria. Proteinuria was 335.6 ± 15.3, 449.9 ± 18.9, and 614.4 ± 23.3 mg / l, respectively, when he underwent single, double, and triple disease.
2. There is a correlation between CHF conditions between proteinuria indicators and the number of comorbidity and fibrosis markers. Proteinuria and comorbidity also increased in sync with aldosterone and TGF-b1.
3. Complex therapies with alzysirtan and eplerenone potency in patients with CHF result in functional depletion of proteinuria and fibrosis markers. A high reliable result is observed when the disease is accompanied by a single comorbid disease.
4. When SYUE is associated with various comorbid diseases, the patient's physical endurance, clinical condition, and quality of life deteriorate according to their number.After the complex treatments performed, the physical loads are extended to 88 when one comorbid condition is detected, 88 and 12.9 meters, respectively, when two and three comorbid conditions are detected. The indicators of quality of life and clinical condition decreased by 23.4 27.1, 24.3 and 2.0 1.72 0.2 points, respectively, and changed for the better.

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