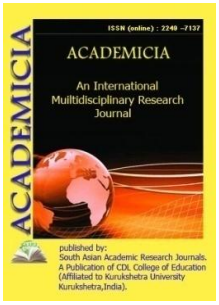
ACADEMICIA

ISSN: 2249-7137 Vol. 11, Issue 4, April 2021 Impact Factor: SJIF 2021 = 7.492

ACADEMICIA
An International Multidisciplinary Research Journal
(Double Blind Refereed & Peer Reviewed Journal)



DOI: 10.5958/2249-7137.2021.01278.7

ASSESSMENT OF THE BALANCE OF INTRA-CARDIAC HEMODYNAMICS AND GLOMERULAR FILTRATION IN ANEMIA WITH DIFFERENT HEMODYNAMIC TYPES OF CHRONIC HEART FAILURE

Feruza Abdujalolovna Xalilova*; Mironshox Dilshodovich Kodirov**

*Assistant,
Department of "Pro-paedeutics of Internal Diseases",
Bukhara Medical Institute,
UZBEKISTAN

**5th Year Student,
Bukhara State Medical Institute,
UZBEKISTAN

ABSTRACT

Renal fibrosis markers were evaluated in dynamics to study specific changes in the kidneys of patients with different hemodynamic types and functional classes of chronic heart failure with anemia and to evaluate the effectiveness of complex treatment. Renal fibrosis marker TGF-$\beta_1$levels in the blood were 2591.0±108.4 and 755.0±18.87 pg / ml, respectively, in chronic heart failure with anemia and without anemia ($p<0.01$). This was indicative of a fibrosis process occurring in the kidney. After complex treatments with the addition of iron, the TGF-β_1 index decreased by 2.25 times ($p<0.01$), the clinical condition, quality of life and resistance to physical exertion changed significantly positively.

KEYWORDS: *Chronic Heart Failure, Chronic Kidney Disease, Renal Dysfunction, Fibrosis Markers, Cystatin-S, TGF-B_1, Ferro-Kinetic Indicators, Galectin-3, Hemodynamic Types.*

INTRODUCTION

Chronic heart failure is one of the leading causes of morbidity and mortality in the world and a disease of significant social and economic importance. Despite advances in the treatment of cardiovascular disease over the past 20 years, this serious complication remains an unresolved

clinical problem. According to the epidemiological survey, the prevalence of chronic heart failure ranges from 0.4% to 2% in the U.S. and European countries, a significant increase with age, reaching 10% in those over 60 years of age.

At the same time, the incidence of chronic heart failure on the planet has been steadily increasing, reaching a level comparable to the most dangerous infectious epidemic diseases in terms of scale and speed of spread (1). About 5.8 million people in the United States and 23 million in the world suffer from Chronic Heart Failure (7.S. 9-13).

It is known that the development of systemic organ damage in CHD, the remodeling of the left ventricle of the heart from its earliest period plays an important role (16. S 107-110).

THE MAIN FINDINGS AND RESULTS

According to the recommendations of the European Society of Cardiologists (ESC 2016), from 2016, patients with CHD are divided into 3 groups, taking into account hemodynamic disorders. According to the indicators of the left ventricular hematopoietic fraction, its reduced (<40%), intermediate (40-49%) and preserved (≥50%) types are distinguished. The standard composition of pharmacological treatment gives a relatively positive result in patients with a decrease in blood drive fraction. In contrast, almost no positive effect is observed in standard pharmacological treatments, with the exception of nitrates in the CHD where the driving fraction is preserved. Therefore, the decompensation phase of the disease leads to negative consequences in almost all cases. Indeed, a number of authors have suggested that left ventricular diastolic filling disorders play a more important role in the pathogenesis of CHD than systolic dysfunction, the severity of the disease, and its consequences. The process of diagnosing diastolic SLE is complex and its pathophysiology has not been fully studied (12 pp. 1444 - 1451; 6 pp. 1-12; 3 pp. 36–46; 15 pp. 1742-1749; 10 pp. 1354-1360).).

As mentioned above, in addition to the prevalence of CHD, it is distinguished from a number of other diseases by its adverse effects and high rate of disability [13]. The average 5-year mortality rate in the population of patients with CHD (I-IV FS) was 59% in men and 45% in women, and was 6-7 times higher than in the general population of the same age (5s.20-26 88s-99- 107.58 pp. 27-36). This is because the degree of damage to the myocardium, along with other organs and systems, ie comorbidity, plays an important role in this complication, which determines the fate of patients and the consequences of the disease (15 p.93–102). Among them, anemia has a special place and is often accompanied by CHD (2016; 11 (1): 37–46). Anemia not only exacerbates the symptoms of CHD, but also worsens quality of life by prolonging hospitalization, reduces resistance to physical exertion, and increases the risk of death by 2 or more times (175 pp.93-102). It should be noted that there is a weak (weak) feedback between hemoglobin and the left ventricular blood drive fraction (28.p.106).

A number of observations have shown that in patients with CHD, anemia is an independent risk factor, in which myocardial oxygen supply is significantly reduced (176 pp. 101–106).

It is known that in addition to anemia, a number of other polymorbid diseases are also detected in patients with CHD. Among them, renal dysfunction plays a leading role not only in the pathogenesis and development of CHD, but also in the exacerbation of anemia (48 pp. 13-24). (2014. T. 112. № 8. S. 7-37.)

THE AIM OF THE STUDY

To evaluate the effectiveness of antianemic therapy based on standard therapy in renal and cardiac fibrosis processes in patients with different hemodynamic types of chronic heart failure with anemia (preserved interval and low).

MATERIALS AND METHODS OF RESEARCH

The 120 patients with CHD involved in the study were divided into 2 groups (75 of them with anemia and 45 without anemia) and underwent excellent clinical and laboratory examinations. In order to carry out the tasks set before us, 75 patients with CHD anemia were divided into 3 groups (in each group there were 25 left ventricular hemorrhage fractions, intermediate and low ones). Their ages ranged from 50 to 70, with an average of 64.0 ± 5.0. All patients were followed up in an outpatient setting after treatment in a hospital setting. The clinical classification of the patients in follow-up is given in Table 1.

TABLE 1 CLASSIFICATION OF PATIENTS INVOLVED IN THE STUDY

№	Indicators	Group I n=75		Group II n=45	
		Absolutely	%	Absolutely	%
1.	Men	32	42,7	25	
2.	Women	43	57,3	20	55,5
3.	Ischemic heart disease	45	60.0	36	44,5
4.	Ischemic heart disease, post-infarction cardiosclerosis	25	33,4	8	17,8
5.	Hypertension	5	6,6	1	2,2
6.	Obesity	12	16	11	24,5

Group I patients were given 200 mg of iron III hydroxide sucrose complex (venofer) intravenously as an antianemic treatment based on standard treatment of CHD during hospital treatment. The total dose of the drug administered to eliminate iron deficiency, using a special formula adopted for the treatment of venofer [total iron deficiency = body weight, kg x (150 - patient hemoglobin index Hb, g / l) x 0.24 + 500 mg] calculated.

Group II patients were prescribed the generally accepted standard treatment for CHD.

As standard treatment for CHD, patients in both groups received angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists, b-adrenoblockers, and mineralocorticoid receptor antagonists (as an eplerenone-antifibrosis drug).

The diagnosis of CHD and its functional classes in the patients included in the study were determined on the basis of their complaints, anamnesis, objective examination and laboratory-instrumental examinations, and according to the criteria of the New York Heart Association (New York Heart Association, 1964).

It was also based on the recommendations of the World Health Organization (hemoglobin <13.0 g / dl for men and <12.0 g / dl for women) as the primary criterion for anemia in group I patients.

RESULTS AND ANALYSIS

Serum ferrokinetic parameters, cardiac and renal fibrosis markers, hemodynamic types, and the presence or absence of anemia were compared in all groups of patients involved in the study. Information about them is given in Table 2.

TABLE 2 DIFFERENT HEMODYNAMIC TYPES OF CHRONIC HEART FAILURE ARE INDICATORS OF CARDIAC AND RENAL FIBROSIS AND GLOMERULAR FILTRATION RATE IN THE ABSENCE OF ANEMIA AND ANEMIA

Indicators	Patients with chronic heart failure anemia and anemia								
	Patients with left ventricular hemorrhage and anemia n = 25> 50%	Patients with left ventricular hemorrhage and n = 15> 50%	P	Patients with left ventricular hemorrhage fraction intermediate and anemia n = 25> 40% = <50%	Patients with left ventricular hemorrhage fraction intermediate and incomplete n = 15> 40% = <50%	P	Patients with decreased left ventricular hemorrhage and anemia n = 25 <40%	Patients with reduced left ventricular hemorrhage and incontinence n = 15 <40%	P
Hemoglabin - g / l	98,5±1,2	139,9±2,0	<0,001	98,6±1,3	134,9±1,6	<0,001	98,5±1,2	139,9±2,0	<0,001
Iron - mk. mol / l	9,7±0,6	25,1±0,8	<0,001	9,4±0,8	22,7±0,6	<0,001	7,9±0,6	22,1±1,0	<0,001
Ferritin - mkg / l	202,3±14,9	332,5±30,5	<0,001	200,4±18,5	352,0±10,4	<0,001	101,0±3,3	363,0±15,9	<0,001
Transferin - g / l	3,92±0,24	4,3±0,3	<0,001	4,2±0,2	3,7±0,2	<0,05	4,8±0,3	3,6±0,37	<0,001
Gale	22,54±1,	19,23±1,	<0,0	19,55±	18,48±	<0,0	19,02±	13,37±	<0,0

ctin - ng / ml	1	12	5	1,3	1,5	5	1,17	1,4	5
Alde stero ne- pg / ml	566,7±14 ,3	526,6±13 ,8	<0,0 5	529,04 ±15,4	468,7± 23,8	<0,0 5	485,2± 14,4	406,3± 20,3	<0,0 5
TGF -β1- pg/m l	2554,7±1 25,4	2209,4±1 22,2	<0,0 5	2832,7 ±176,0	2194,3 ±75,8	<0,0 5	2332,8 ±167,8	1994,2 ±73,1	<0,0 5
Cyst atin S mg / l	1,39±0,0 5	1,25±0,0 5	<0,0 5	1,58±0, 15	1,19±0 ,12	<0,0 5	1,32±0 ,12	1,26±0 ,02	<0,0 5
Ball filtra tion ml / min	65,6±2,4 5	68,4±2,3	<0,0 5	67,8±2, 64	72,8±1 ,17	<0,0 5	58,2±1 ,7	69,95± 1,05	<0,0 5
Sodi um - m.m ol / l	136,28±1 ,73	132,8±1, 6	<0,0 5	138,24 ±1,72	141,2± 1,2	<0,0 5	135,42 ±1,3	143,6± 1,14	>0,0 5
Potas sium - m.m ol / l	7,86±0,5	7,9±0,5	<0,0 5	7,47±0, 46	7,9±0, 6	<0,0 5	7,5±0, 5	7,9±0, 62	<0,0 5
Chlo rine ml.m ol / l	104,1±1, 56	103,4±1, 5	<0,0 5	105,32 ±1,5	108,7± 1,12	<0,0 5	106,2± 1,45	109,7± 1,13	<0,0 5

In the groups where the left ventricular hemorrhage fraction was maintained and anemic, hemoglobin, iron, ferritin, and transferrin levels were found to be 29.6%, 61.3%, 39.1%, and 8.8% lower ($p < 0.001$), respectively, than in non-anemic groups. The left ventricular hemorrhage fraction was 26.9%, 55.8%, 43.1%, 13.5% in the intermediate group, and 29.5%, 64.2%, 72.1%, and 33.3% in the decreased ventricular fraction decreased, respectively, with a reliable difference ($p < 0.001$). These indicators indicate that patients are reliably distributed in groups based on hemoglobin indicators.

In recent years, galectin-3 has been proven to be a reliable marker of fibrosis in pathological processes in the body and primarily in the heart. However, although this marker has been studied in CHD, there is no data in the available literature on its change in anemia. In the left ventricular

hemorrhage fraction observed in our observations, in the intermediate and decreased groups, when they passed with anemia and without anemia, the galectin-3 values were 22.5 ± 1.1 and 19.23 ± 1.1, 19.55 ± 1.3 and 18.5 ± 1.5, 19.02 ± 1.2, and 13.2 ± 1.4, respectively. ng / ml was equal to ($p < 0.05$). At the same time, its indicators were 1.2, 1.1 and 1.4 times higher in different hemodynamic types, respectively, than in those who did not have anemia.

It is known that aldosterone is actively involved not only in water-salt metabolism in the body, but also in fibrous processes, which has been proven in numerous studies. In recent years, there have been reports that this hormone is produced not only in the adrenal glands, but also in other internal organs, including the kidneys and heart. Numerous studies have been conducted on the modification of CHD under the influence of various FS and a number of drugs. However, data on aldosterone levels in the blood are insufficient when this severe complication occurs in comorbidity with anemia. In this context, we studied its indications in patients with CHD anemia and anemia.

At the same time, aldosterone was 1.1, 1.1, and 1.2 times ($p < 0.05$) significantly higher in patients with left ventricular hemorrhage, interstitial, decreased, and anemia than in non-anemic patients, respectively. The indicators confirm that not only the hemodynamic types of CHD but also the presence of anemia increases aldosterone in the blood, and therefore fibrous processes increase.

TGF-$\beta_1$plays a leading role in the development of fibrous processes in the body and primarily in kidney tissue. However, there is insufficient data in scientific sources on the change of this cytokine in CHD with anemia. In patients with left ventricular hemorrhage fraction, intermediate, decreased, and anemia and anemia without follow-up, TGF-b1 values were 2554.7 ± 125.4 and 2209.4 ± 122.2 ($p < 0.05$), 2832.7 ± 176.0, and 2194.3 ± 75.8 ($p < 0.05$), respectively. , 2332.8 ± 167.8 and 1994.2 ± 73.1 pg / ml ($p < 0.05$).

Cytokine levels were 13.5%, 22.5%, and 14.5%, respectively, in the presence of anemia and in the absence of anemia.

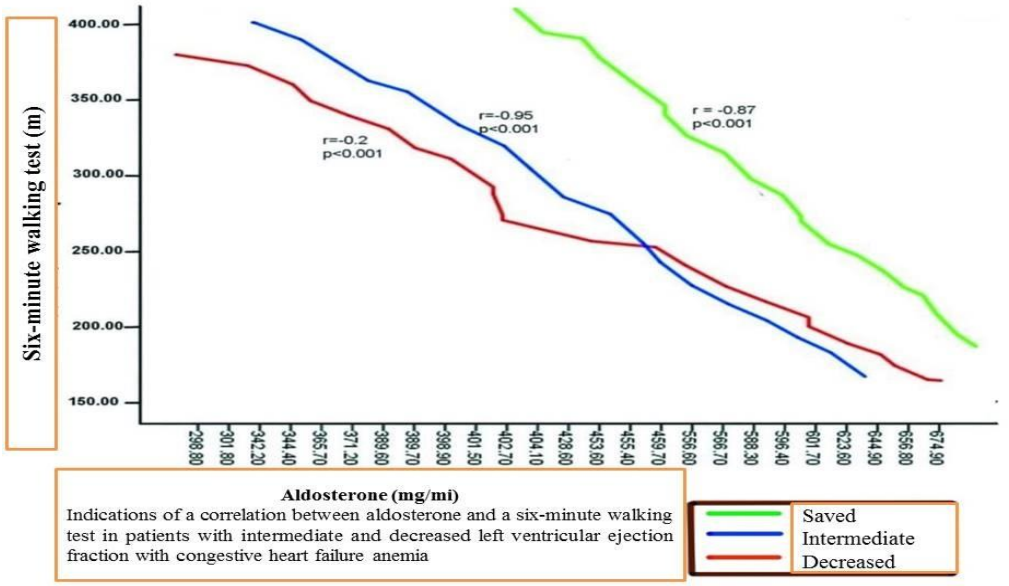
It is known that in recent years, special attention is paid to cystatin-C in the assessment of renal function. It has a number of advantages over creatinine. Therefore, we determined cystatin-C levels in the blood of patients in our follow-up and assessed glomerular filtration using it. Cystatin-C rates were 10.1%, 24.6%, and 4.54% higher, respectively, in patients with left ventricular hemorrhage fraction, intermediate, decreased, and anemic groups than in anemic patients.

It has been shown that early development of fibrous processes in the kidneys of patients with anemia and the process adversely affects the functional state of the kidneys.

Cystatin-C-assisted glomerular filtration rates also confirm these changes, i.e., a significant decrease ($p < 0.05$) of 4.3%, 7.4%, and 20.2%, respectively, compared with non-anemics when anemia was detected in all hemodynamic types.

In the next phase of our study, the correlation between cardiac and renal fibrosis markers and fibrosis markers with the identified ferrokinetic parameters was studied. The relationship between the 6-minute walking test and aldosterone levels among all hemodynamic types of CHD with anemia is shown in Figure 1.

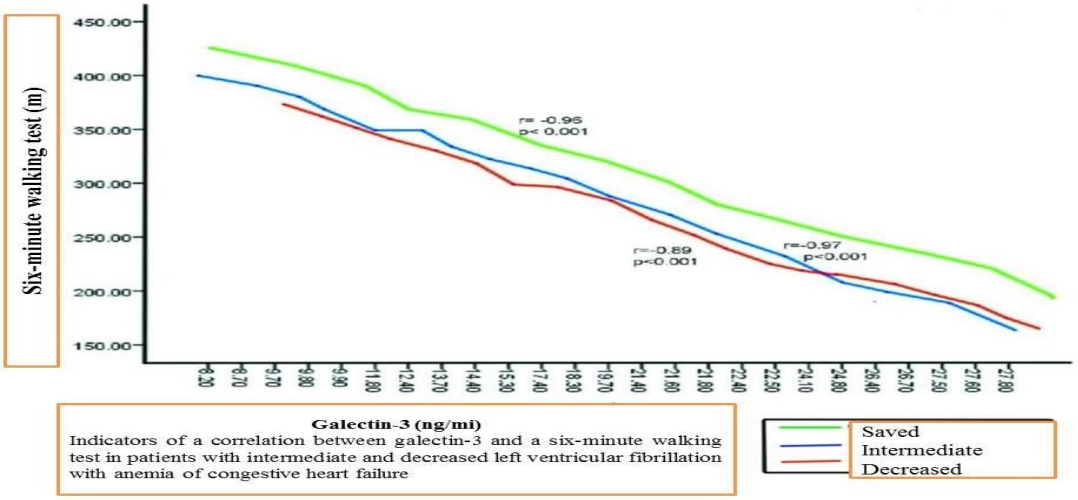
FIGURE 1



In which the left ventricular hemorrhage fraction was preserved, the correlation between the indicators recorded in intermediate and decreased patients was r = - 0.87, respectively; p <0.001, r = - 0.95; p <0.001 and r = - 0.2; p <0.01. In all cases, a reliable negative correlation was found between aldosterone and the 6-minute walking test. This confirms that an increase in aldosterone in the blood, which is one of the markers of fibrosis in the kidneys and heart, has a convincing negative effect on patients 'resistance to loads.

Also, among all hemodynamic types of CHD with anemia, the correlation between the 6-minute walking test and galectin-3, which is a reliable marker of fibrous processes in the heart, was r = - 0.95, respectively; p <0.001, r = - 0.97; p <0.001 and r = - 0.89; p <0.01 was equal to (Figure 2).

FIGURE 2

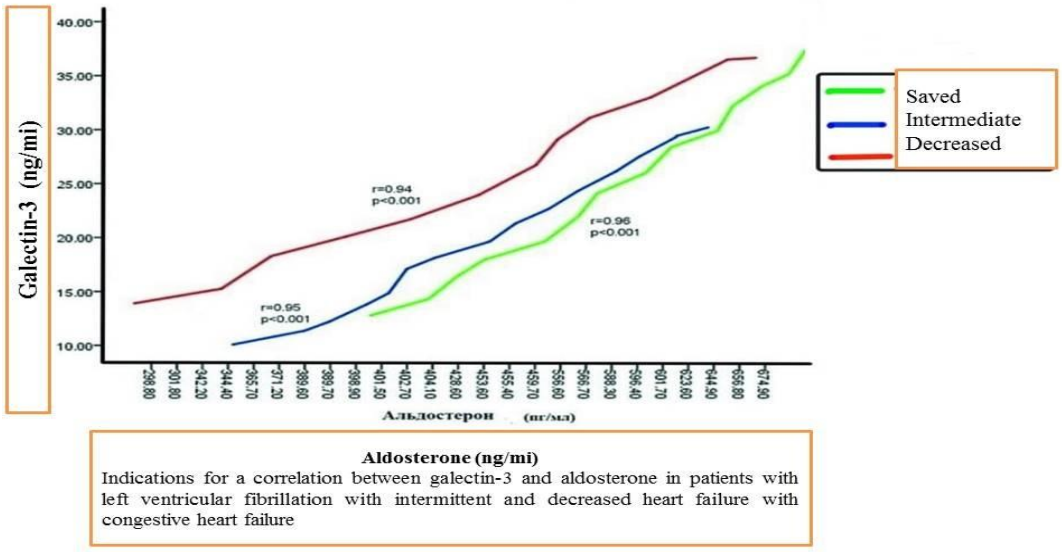


This analysis showed that there was a reliable inverse relationship with galectin-3 in all hemodynamic types and in 6-minute walking synapses.

Although the figures in Figures 1-2 above showed a reliable correlation between fibrosis markers in all types of CHD and patient resistance to physical activity, the high correlation was more pronounced in CHD left ventricular hemorrhage fraction preserved and in intermediate types (respectively r = - 0.87; p <0.001, r = - 0.95; p <0.001 and r = - 0.95; p <0.001, r = - 0.97; P <0.001). These results confirm the data in the literature on the fact that the diastolic type of CHD is accompanied by more fibrous processes.

In the next step, we studied the interaction between galectin-3 and aldesterone, which are reliable markers of fibrosis processes in the body (Figure 3).

FIGURE 3



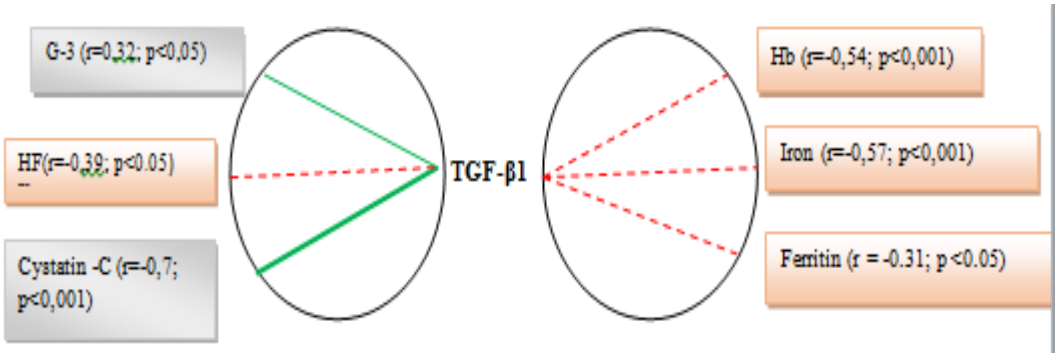
Aldosterone (ng/mi)
Indications for a correlation between galectin-3 and aldosterone in patients with left ventricular fibrillation with intermittent and decreased heart failure with congestive heart failure

As shown in the diagram, these markers have a mutually reinforcing effect on each other, so an increase in one leads to an increase in the other. This process is confirmed by the existing positive correlation between them in all hemodynamic types of CHD (r = 0.94; p <0.001, r = 0.95; p <0.001 and r = 0.96; p <0.001, respectively). Therefore, when CHD is observed with anemia, fibrous processes in the body coexist and have a strengthening effect on each other.

A reliable negative correlation was also found between ferritin and fibrosis markers galectin-3 and aldosterone (r = - 0.43; p <0.05 and r = -0.42; p <0.05) in the group with anemia in which the CHD hemorrhage fraction was preserved.

In the next stage, patients with CHD anemia and decreased left ventricular hemorrhage fraction were identified in the blood and correlated with ferrokinetic indicators and cardiac fibrosis marker galectin-3 and cystatin-C, widely used in recent years in the assessment of renal functional status; with TGF-$\beta_1$we studied the dependencies (Figure 4).

FIGURE 4



HF - hemorrhage fraction

Correlation between TGF-$\beta_1$and ferrokinetic parameters, galectin-3, cystatin-C, and hemorrhagic fraction in patients with decreased left ventricular hemorrhage fraction in chronic heart failure anemia

As shown in Figure 4, an increase in TGF-$\beta_1$in the blood leads to a reliable decrease in the left ventricular hemorrhage fraction (r = -0.39; p <0.05). It was also noted that TGF-b1 is negatively correlated with ferrokinetic parameters. In this case, it is correspondingly with a hemoglobin index r = -0.54; p <0.001, with serum iron r = -0.57; p <0.001, with ferritin r = -0.31; p <0.05 was detected. These indicators confirm that the renal fibrosis marker interacts with the markers confirming anemia, leading to the development of fibrous processes.

A study of ferrokinetic factors affecting ball filtration rate (BFR) revealed a number of correlations as shown in Figure 5. In particular, an increase in hemoglobin in the blood leads to a parallel increase in BFR (r = 0.517; p <0.01). A similar correlation was observed between CFT and serum iron and ferritin (r = 0.66; p <0.001) and (r = 0.45; p <0.05), respectively. These figures confirm that a positive correlation between ferrokinetic parameters and BFR has a positive effect on renal function (Figure 5). Therefore, the elimination of iron and ferritin deficiency in the body has a positive effect on the functional state of the kidneys, stabilizes the general condition of patients and improves quality of life.

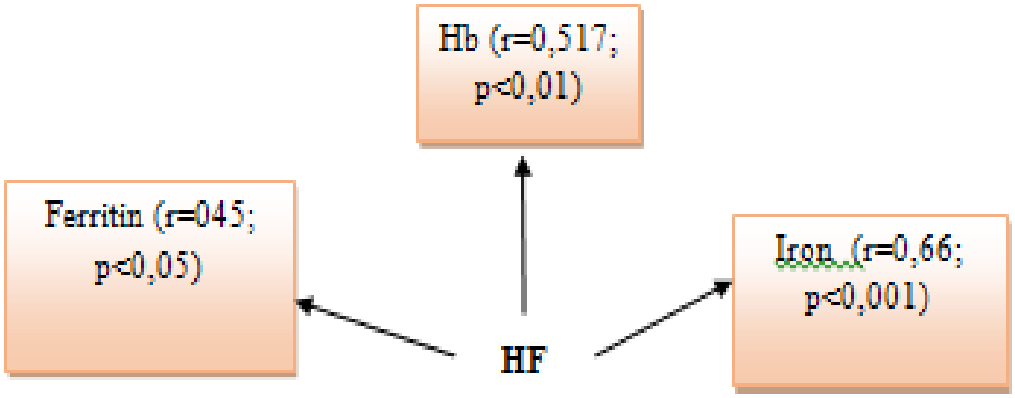


FIGURE 5

Correlation between the rate of glomerular filtration rate and ferrokinetic parameters in patients with decreased left ventricular hemorrhage fraction in anemia with chronic heart failure.

The association between cystatin-C and ferrokinetic parameters, which have been widely used in the assessment of renal functional status in recent years, has shown that an increase in it in the blood leads to an increase in anemia.

In particular, an increase in cystatin-S in the blood leads to a reliable decrease in hemoglobin (r = -0.30) and serum iron and ferritin (r = -0.48 and r = -0.29) (p <0.05 in all cases) (Figure 6).).

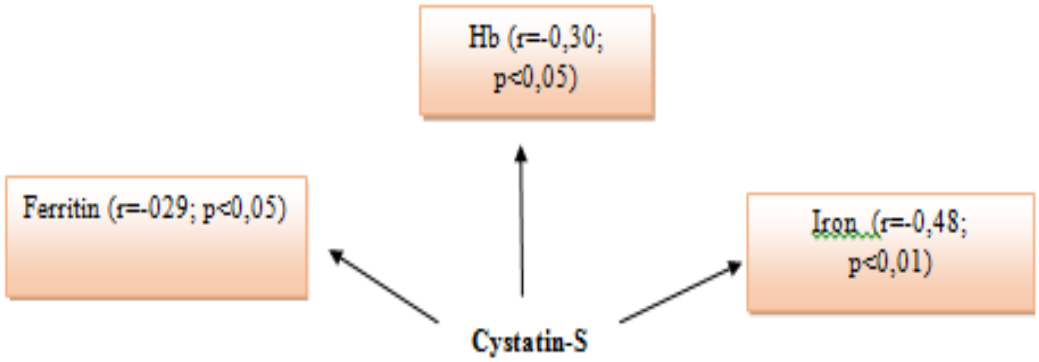


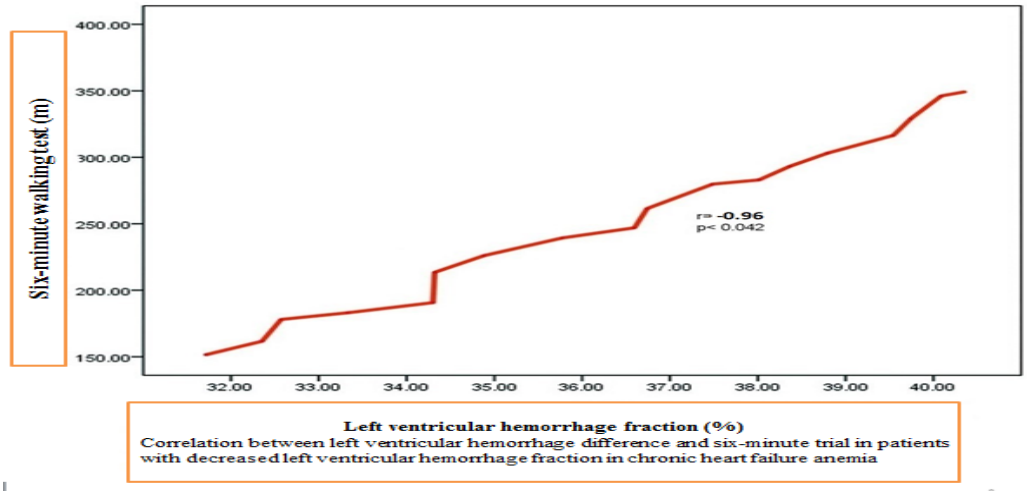
FIGURE 6

Correlation between cystatin-C and ferrokinetic parameters in patients with decreased left ventricular ejection fraction with chronic heart failure anemia

The results confirm that anemia is synchronized with an increase in cystatin-C levels in the blood and that they have an aggravating effect on each other.

It was also found that there was a negative correlation (r = -0.96; p <0.01) between the hemorrhage fraction and the endurance index in patients with decreased left ventricular hemorrhage fraction (Figure 7).

FIGURE 7



It has been proven in numerous studies that a decrease in the left ventricular hemorrhage fraction leads to a decrease in the level of endurance of patients to physical exertion.

The results confirmed that galectin-3 and TGF-β_1, which indicates fibrosis processes in the heart and kidneys, and aldosterone, a marker of fibrosis in both organs, increased in parallel when CHD was associated with anemia. At the same time, the increase in the marked markers was more pronounced in the CHD hemorrhage fraction was preserved and in the intermediate hemodynamic types, ie diastolic dysfunction. In cases where CHD was accompanied by a decrease in left ventricular hemorrhage fraction, a clear reliable negative correlation between renal fibrosis marker TGF-b1 and cystatin-S and ferrokinetic parameters was found. This confirms that the development of fibrous processes when CHD is accompanied by anemia and an excess of cystatin-C in the blood leads to an exacerbation of existing anemia. The results show that monan antianemic and antifibrosis treatments should be performed on the basis of standard treatment in CHD with anemia.

CONCLUSION

1. An increase in galectin-3 levels in the blood led to a reliable decrease in the six-minute walking test in all hemodynamic types (preserved, intermediate, and decreased) with chronic heart failure anemia.

2. A positive reliable correlation between aldosterone and galectin-3 confirmed in all hemodynamic types of chronic heart failure with anemia confirmed the synchronization of fibrous processes in the body.

3. An increase in galectin-3 in the blood resulted in a correspondingly reliable decrease in the six-minute walking test in all hemodynamic types (preserved, intermediate, decreased) with chronic heart failure anemia.

4. Negative correlation between TGF-b1 and ferrokinetic parameters, i.e. hemoglobin, iron and ferritins, they have been shown to have a mutually reinforcing effect.

5. High levels of aldosterone were detected in patients in the group where the left ventricular hemorrhage fraction was maintained.

REFERENCES

1. Atroshenko E. S. (2007) *Patient with chronic heart failure and preserved systolic function of the left ventricle* / E. S. Atroshenko // Heart failure. – Tashkent: 8. - 6. –pp. 297-300. (Atroshenko Ye. S. Pasient s xronicheskoy serdechnoy nedostatochnost'yu i soxranennoy sistolicheskoy funksiey levogo jeludochka / Ye. S. Atroshenko // Serdechnaya nedostatochnost'. – 2007. – T. 8. – 6. – S. 297-300.)
2. Belyalov F.I. (2012)*Treatment of internal diseases in conditions of comorbidity: monograph*. / F.I.Belyalov. - 8th ed. - Irkutsk: RIO Igiuva. – p. 285. (Belyalov F. I. Lechenie vnutrennix bolezney v usloviyax komorbidnosti: monogr. / F. I. Belyalov. – 8-e izd. – Irkutsk: RIO IGIUVa, 2012. – 285 S.)
3. Gadaev A.G., Turakulov R.I., Kurbonov A.K. (2019) Occurrence of anemia in chronic heart failure and its negative impact on the course of the disease // *Medical Journal of Uzbekistan*. 2. – pp. 74 - 77. (Gadaev A.G., Turakulov R.I., Kurbonov A.K. Surunkali yurak

yetishmovchiligida kamqonlikni uchrashi va uni kasallik kechishiga salbiy ta'siri // O‘zbekiston tibbiyot jurnali. – 2019 – 2. – S. 74 – 77.)

4. Gadaev A.G, Qurbonov A.K, Sabirov M.A, Sayfullayev M.B, Gadaeva N.A., Turakulov R.I. Assessment of Erythropoietin Levels and Correlation with Cytokines in Patients with Chronic Heart Failure // *International Journal of Pharmaceutical Research*. – 2021. - Vol 13P. 713-720.
5. Naumova L.A., Osipova O.N. (2016). Comorbidity: mechanisms of pathogenesis, clinical significance // *Modern problems of science and education*. 5. - pp. 19-26. (Naumova L.A., Osipova O.N. Komorbidnost': mexanizmi patogeneza, klinicheskoe znachenie // Sovremennie problemi nauki i obrazovaniya. – 2016. – 5. – S. 19-26.)
6. EwansW. E. Pharmacogenomics – DrugDisposition, DrugTargets, and Side Effects / W. E. Ewans, H. L. McLeod // N. Eng. J. Med. – Vol. 3. – 2003. – Feb. – Vol. 48, N 6. – pp. 538-549.
7. Bayliss E. A. Description of barriers to self-care by persons with comorbid chronic diseases / [et al.] // *Annals of Family Medicine*. – 2003. – Vol. 1. – 1. – pp. 15-21.
8. 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. – pp. 413-419.
9. Fortin M. [et al.]. A systematic review of prevalence studies on multimorbidity: Toward a more uniform methodology // Annals of Family Medicine. – 2012. – Vol. 10. – 2. – P. 142-151.
10. Longjian L. *Epidemiology of heart failure and scope of the problem* // Cardiology Clinics. – 2014. – Vol. 32. – pp. 1-8.
11. Garganeeva A.A., Bauer V.A., Borel K.N. (2014) Pandemic of the XXI century: chronic heart failure - the time of modern society. Epidemiological aspects // *Siberian medical journal (Tomsk).* – pp. 8-12; E-mail: borel.ks@ya.ru. (Garganeeva A.A., Bauer V.A., Borel' K.N. Pandemiya XXI veka: xronicheskayaserdechnayane dostatochnost' – vremyasovremennogoobshestva. Epidemiologicheskieaspekti // Sibirskiymedisinskiyjurnal (Tomsk). – 2014. – S. 8-12; E-mail: borel.ks@ya.ru.)
12. Vertkin A.L., Rumyansev M.A., Skotnikov A.S. *Comorbidity in clinical practice*. Part 1. - 2011. Arxiv of Internal Medicine. - 2011. - (1). – pp. 16-20. (Vertkin A.L., Rumyansev M.A., Skotnikov A.S. Komorbidnost' v klinicheskoypraktike. Chast' 1. – 2011. Arxivvnutrenneymedisini. – 2011. – (1). – S. 16-20.)
13. Fortin M., Bravo G., Hudon C. etai. (2005) *Prevalence of multi-morbidity among adults seen in family practice* // Ann. Fam. Med. 3. – pp. 223-8.
14. Efremova Yu. E. (2015) *Treatment of edematous-syndromaprichronic heart failure.* Breast cancer. 27. – pp. 1622-1624 (YefremovaYu.E. Lechenieotechnogosindromaprixronicheskoyserdechnoynedostatochnosti. RMJ. – 2015 – 27. S. 1622-1624.)
15. Shah A.D., Langenberg C., Rapsomaniki E., et al. (2015) Type 2 diabetes and insaides of cardiovascular diseases: a cohort study 1,9 million people. Lancet Diabetes Endocrinol. 3. – pp. 105-13.
16. Lypez-Sendyn J. (2011) *The heart failure epidemic* // Medio-graphia. Vol. 33. – pp. 363-369.
17. Shutov A.M., Efremova E.V. (2015)*Clinical features, quality of life, prognosis of patients with chronic cardiorenal syndrome* // Nephrology. – Tashkent: 19. - 2. - p. 64. (Shutov A.M.,

YefremovaYe.V. Klinicheskieosobennosti, kachestvojizniiprognozbolnix s xronicheskimkardiorenalnimsindromom // Nefrologiya. – 2015. – T. 19. – 2. – S. 64.)

18. Lazebnik L.B. (2005) *Aging and polymorbiticity*// Medical Consilium. 12. - pp. 993-996. (Lazebnik L.B. Starenieipolimorbitnost' // Consiliummedicin – 2005. – 12. – S. 993-996.)

19. Sharabchiev Yu.T., Antipov V.V., Antipova S.I. (2014) *Comorbidity - an actual scientific and scientific-practical problem of medicine in the XXI century* // Medical news. 8. - pp. 6-11. (SharabchievYu.T., Antipov V.V., Antipova S.I. Komorbidnost – aktualnayanauchnaya I nauchno-prakticheskayaproblemamedisini XXI veka // Medisinskienovosti – 2014. – 8. – S. 6-11.)

20. Gubanova G.V., Belyaeva N., Shemetova G.N. (2015) Comorbid patient: stage of formation, risk factors and management tactics // *Modern problem of science and education*. 6. URL: xttp: // science-education.ru/article/ viev? Id = 23986. (Gubanova G.V., BelyaevaYu.N., Shemetova G.N. Komorbidniypasient: etapiformirovaniya, faktoririskaitaktikavedeniya // Sovremennie problem naukiiobrazovaniya. – 2015. – 6. URL:http:// science-education.ru/article/ view?id=23986.)

21. Shukurov R.T., Abdullaev T.A. (2017) Gender differences and comorbidity in patients with chronic heart failure // *Cardiovascular therapy and prevention*. 16 (6). –pp. 87-91. (Shukurov R.T., Abdullaev T.A. Gendernierazlichiyai komorbidnost u bolnix s xronicheskoyserdechnoy nedostatochnostyu // Kardiovaskulyarnayaterapiyaiprofilaktika. – 2017. 16(6). – S. 87-91.)

22. Roig E. La анемияEn La Insuficienciacardiaca. їEsOOHmarcadorдegravedadoobjetivoterapйuticoOOH? // Rev EspCardiol. – 2005. – Vol. 58. – P. 10-12.

23. Sharma R., Anker S. D. (2001) The 6-minute walk test and prognosis in chronic heart failure-the available evidence // Eur Heart J. Vol. 22. - pp. 445-448.

24. Ni H., Toy W., Burgess D. et al. Comparative responsiveness of short – Form 12 and Minnestota Living With Heart Failure Questionnare in patients with heart failure // *J. Card. Failure*. - 2000. - Vol. 6, №2. - pp. 83-91.

25. Mareev V. Yu. Results of the most interesting research on the problem of cardiac sufficiency in 1999 // *J. Heart failure*. - 2000. - Volume 1, No. 1. - pp. 8-17. (Mareev V. Yu. Results naibolee interesnyx issledovaniy po problem serdechnoyne dostatochnosti v 1999 godu // J. Serdechnaya nedostatochnost. - 2000. - Tom.1, №1. - S. 8-17.)

26. Tosheva Khakima Bekmurodovna, Erkinova Nigora Erkinovna, Gadaev Abdigaffar Gadaevich, Djuraeva Nozima Oripovna, Khalilova Feruza Abdujalolovna. Comorbid States in Patients with Chronic Heart Failure. Regional Level of the Problem (Preliminary Study) //*Journal of Cardiovascular Disease Research*. – 2020 – Vol. 11, - pp. 59-65.

27. ToshevaKh.B., Xalilova F.A., Gadaev A.G., Erkinova N.E., Djuraeva N.O. Impact Of Chronic Heart Failure On Comorbidities In Hot Climates On The Quality Of Life And Clinical Condition Of Patients // *European Journal of Molecular & Clinical Medicine*. -2020 – Vol. 7, - pp. 1080-1089.

28. Gadaev A.G., Tosheva X.B., Elmuradov F.X., Xalilova F.A. Fibrous changes in the kidneys in patients XSN. *Therapy Bulletin of Uzbekistan*. 2018. - pp. 86 - 90.

29. Gadaev A.G., Xalilova F.A., Elmuradov F.X., Tosheva X.B. Structural and functional changes in the kidneys and heart in patients with XSN. *Therapy Bulletin of Uzbekistan*. 2018. -1. – pp. 100-104.

30. Roig E. (2005) La anemia Yong La Insuficiencia sardias. ïEsOOH marcador gegravedado having burned the UN therapy? // Rev Espardiol. Ox. 58. - pp. 10-12. (Roig E. La анемия En La Insuficiencia cardiaca. ïEsOOH marcador degravedado objetiv oterapйutico OOH? // Rev EspCardiol. – 2005. – Vol. 58. – P. 10-12.)

31. Fortin M., Bravo G., Hudon C. etai. (2005) Prevalence of multi-morbidity among adults seen in family practice // Ann. Fam. Med. 3. – pp. 223-8.

32. O'Meara E, Clayton T, McEntegart MB, McMurray JJ, Lang CC, Roger SD, Young JB, Solomon SD, Granger CB, Ostergren J, Olofsson B, Michelson EL, Pocock S, Yusuf S, Swedberg K, Pfeffer MA [Anemia and Iron Deficiency in Heart FailureCurrent Concepts and Emerging TherapiesInder S. Anand andPankaj GuptaOriginally published2 Jul 2018https://doi.org/10.1161/CIRCULATIONAHA.118.030099Circulation. 2018;138:80–98;).

33. Mehta RL, Rabb H, Shaw AD, et al. Cardiorenal syndrome type 5: clinicalpresentation, pathophysiology and management strategies from theeleventh consensus conference of the Acute Dialysis Quality Initiative(ADQI). Contrib Nephrol. 2013;182:174–194).

34. Inder S. Anand and Pankaj GuptaAnemia and Iron Deficiency in Heart Failure, Current Concepts and Emerging Therapies/, in Depht, 10.1161/CIRCULATIONAHA.118.030099, Circulation July 10, 2018.

35. Gadaev A.G., Qurbonov A.K., Tosheva X.B., Erkinova N.A., Turakulov R.I. (2019) Principles of treatment of chronic heart failure with anemia // *Bulletin of the Tashkent Medical Academy*. №2. - pp.18 - 21. (Гадаев А.Г., Қурбонов А.К., Тошева Х.Б., Эркинова Н.А., Турақулов Р.И. Сурункали юрак етишмовчилиги камқонлик билан кечганда даволаш тамойиллари // Тошкент тиббиёт академияси ахборотномаси. – 2019. - №2. - С.18 – 21.)

36. Gadaev A.G. Qurbonov A.K., Turakulov R.I. (2019) Occurrence of anemia in chronic heart failure and its negative impact on the course of the disease // *Medical Journal of Uzbekistan*.№2. - pp. 74 - 77. (Гадаев А.Г. Қурбонов А.К., Турақулов Р.И. Сурункали юрак етишмовчилигида камқонликни учраши ва уни касаллик кечишига салбий таъсири // Ўзбекистон тиббиёт журнали.- 2019. - №2. - С. 74 – 77.)

37. Tosheva Kh. B.,Gadaev A. G. *Dynamics of Renal Fibrosis Markers on the Basis of Complex Treatment in Chronic Heart Failure with Anemia* // Psychology and Education. – 2021.- Vol. 3.- P. 1291-1301