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DIASTOLIC DYSFUNCTION OF THE LEFT VENTRICLE IN HIV–INFECTED PATIENTS, CLINICAL AND PROGNOSTIC RELATIONSHIPS

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SUMMARY

Diastolic dysfunction in HIV-infected patients is a common problem, the pathway of which is based on chronic low-intensity inflammation, and whose consequences are associated with progression of chronic heart failure (CHF) and death. The aim of the study was to evaluate clinical, echocardiographic and laboratory data of patients with diastolic left ventricular myocardial dysfunction infected with HIV and to present new prognostic relationships. Within the framework of a one-stage, screening, clinical study in the conditions of a multidisciplinary clinic, 240 patients with HIV infection were examined, and 136 of them showed signs of diastolic dysfunction. The development of diastolic dysfunction in HIV-infected patients is a factor provoking the development and progression of CVD, ventricular rhythm disturbances, ischemic heart disease, and anemia. Diastolic dysfunction in HIV-infected patients increases the risks of death within 2 years by 1.46 times. Increase of NT-proBNP concentration in plasma of HIV-infected patients ≥ 185.7 pg/mL is associated with the development of diastolic dysfunction in them.

KEYWORDS: *HIV infection, diastolic dysfunction, chronic heart failure.*

CONFLICT OF INTEREST. The authors declare no conflict of interest.

ДИАСТОЛИЧЕСКАЯ ДИСФУНКЦИЯ ЛЕВОГО ЖЕЛУДОЧКА У ВИЧ–ИНФИЦИРОВАННЫХ ПАЦИЕНТОВ, КЛИНИЧЕСКИЕ И ПРОГНОСТИЧЕСКИЕ ВЗАИМОСВЯЗИ

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РЕЗЮМЕ

Диастолическая дисфункция у ВИЧ-инфицированных пациентов является распространенной проблемой, в основе которой лежит хроническое воспаление низкой интенсивности и последствия которого связаны с прогрессированием хронической сердечной недостаточности (ХСН) и смертью. Целью исследования была оценка клинических, эхокардиографических и лабораторных данных пациентов с диастолической дисфункцией миокарда левого желудочка, инфицированных ВИЧ, и представление новых прогностических зависимостей. В рамках одноэтапного, скринингового, клинического исследования в условиях многопрофильной клиники было обследовано 240 пациентов с ВИЧ-инфекцией, и у 136 из них были выявлены признаки диастолической дисфункции. Развитие диастолической дисфункции у ВИЧ-инфицированных пациентов является фактором, провоцирующим развитие и прогрессирование сердечно-сосудистых заболеваний, желудочковых нарушений ритма, ишемической болезни сердца и анемии. Диастолическая дисфункция у ВИЧ-инфицированных пациентов увеличивает риск смерти в течение 2 лет в 1,46 раза. Повышение концентрации NT-proBNP в плазме крови ВИЧ-инфицированных пациентов ≥ 185,7 пг/мл связано с развитием у них диастолической дисфункции.

КЛЮЧЕВЫЕ СЛОВА: ВИЧ-инфекция, диастолическая дисфункция, хроническая сердечная недостаточность.

КОНФЛИКТ ИНТЕРЕСОВ. *Авторы заявляют об отсутствии конфликта интересов.*

Introduction

The prevalence of diastolic dysfunction in HIV-infected patients is of concern, because there is a clear association between the development of diastolic dysfunction, chronic heart failure (CHF) and mortality, and the age of patients with first diagnosed diastolic dysfunction is getting younger [1]. The leading role in the pathogenesis of diastolic dysfunction in HIV infection belongs to chronic low-intensity inflammation against the background of constant immune activation [2, 3, 4]. Inflammatory markers remain elevated despite viral load suppression, and the progression of diastolic dysfunction is accompanied by myocardial and arterial stiffness in HIV-infected patients [5], with myocardial inflammation and diffuse myocardial fibrosis clearly identified on cardiac MRI [6, 7]. The aim of the study was to evaluate clinical, echocardiographic and laboratory data of patients with diastolic left ventricular myocardial dysfunction infected with HIV and to present new prognostic relationships.

Materials and methods

In the conditions of a multidisciplinary city hospital, 240 HIV-infected patients with different therapeutic pathology after compensation of the disease that led to hospitalization were examined during four years; signs of diastolic dysfunction were detected in 136 of them. The study is single-stage, clinical, screening and complies with GCP and Declaration of Helsinki criteria. Inclusion criteria were the presence of HIV infection confirmed by immunoblot, signed voluntary consent to participate in the study. Exclusion criteria were patient refusal to participate in the study, oncopathology, and deviant behavior, acute decompensation of CHF or acute heart failure. The author personally performed echocardiography in each patient according to the methodology prescribed in the guidelines for quantitative assessment of the structure and function of heart chambers recommended by the American Echocardiographic Society and the European Echocardiographic Association. All patients were examined physically to detect symptoms and signs of CHF, the severity of detected CHF was assessed using the kinic state assessment scale modified by V.Y. Mareev and the six-minute walk test.

Diastolic dysfunction was determined in accordance with the recommendations for visualization of left ventricular diastolic function on echocardiography proposed by the American Society of Echocardiography and the European Association of Cardiovascular Imaging in 2016 [8], and Tei index was determined by pulsed-wave Doppler peaks. In addition to traditional clinical analyses, the patients underwent: determination of brain natriuretic propeptide (NT-proBNP) concentration in blood plasma by Vector Best reagent sets (Russia), serum levels of transferrin, ferritin, serum iron by RANDOX reagent sets (Great Britain), lipocaine-2 (NGAL) by reagent sets of Sanlong Biotech Co. Ltd (China), C-reactive protein (CRP) by Vector Best reagent kits (Russia). Verification of alcohol dependence was performed by questioning patients with AUDIT questionnaire with ≥ 20 points.

Statistical processing was performed in SPSS 26 and Statistika 13.0 programs. After determining the normality of the distribution of signs according to Kolmogorov – Smirnov and Shapiro – Wilk, signs with normal distribution were prescribed in the form of arithmetic mean and standard deviation (M±SD), signs with irregular distribution – in the form of median, first and third quartiles (Me [LQ; UQ]). Categorical traits were prescribed as absolute value and frequency of occurrence in percentage (n (%)). A statistical significance level of $p<0.050$ was recognized as critical. Mann – Whitney, Kraskell – Wallis, Student's t-criterion, quadratic conjugation tables, odds ratio and risk ratio were used in pairwise comparison of traits.

Results of the study

Table 1 presents the main data characterizing the clinical course of diastolic dysfunction in patients with HIV infection.

Table 1

The main indicators characterizing the clinical features of the course of diastolic dysfunction in HIV-infected people

Sign	Diastolic dysfunction present, n=136	Diastolic dysfunction not determined, n=104	p
Male gender, n (%)	78 (57)	67 (64)	0,267
Age, years	38,00 [34,00; 42,00]	36,00 [32,00; 40,00]	0,114
TSW, m	400 [300; 450]	450 [400; 500]	0,004*
SACC, points	5,0 [4,0; 8,0]	2,5 [1,0; 5,0]	<0,001*
Smoking, n (%)	94 (69)	66 (63)	0,357
Probable alcohol dependence, n (%)	83 (61)	42 (40)	0,001*
Drug usage, n (%)	109 (80)	73 (70)	0,074
IHD, n (%)	31 (23)	7 (7)	<0,001*
History of myocardial infarction, n (%)	4 (3)	0 (0)	0,077
Diabetes mellitus, n (%)	7 (5)	6 (6)	0,832
Atrial fibrillation, n (%)	5 (4)	0 (0)	0,048*
VA, n (%)	50 (37)	14 (13)	<0,001*
Stroke in anamnesis, n (%)	3 (2)	2 (2)	0,879
CABG, PCI in anamnesis, n (%)	1 (0,6)	0 (0)	0,380
Chronic virus hepatitis C, n (%)	97 (71)	69 (66)	0,408
Ascites, n (%)	30 (22)	12 (11)	0,033*
Liver cirrhosis, n(%)	30 (22)	12 (11)	0,033*
Hydropericardium, n(%)	10 (7,35)	4 (4)	0,250
Hydrothorax, n (%)	23 (17)	13 (12)	0,342
ART, n (%)	25 (18)	13 (12)	0,216
BMI, kg/m^2	20,0 [17,7; 21,9]	20,2 [18,4; 22,0]	0,409
Low body weight, n (%)	26 (19)	18 (17)	0,839
Valve defects, n (%)	36 (26)	18 (17)	0,092
Esophageal candidiasis, n (%)	12 (9)	5 (5)	0,229
Unsuppressed viral load	130 (95,59)	6 (5,77)	<0,001
Death within 2 years	22 (16,17)	6 (5,77)	0,012*

Abbreviations: * – differences in indicators are statistically significant (p <0.05); TSW – six-minute walk test; SACC – scale for assessing the clinical condition of patients with CHF, modified by V.Yu. Mareev; VA – Ventricular arrhythmias; CABG – coronary artery bypass grafting; PCI – percutaneous coronary intervention; ART – antiretroviral therapy; BMI – body mass index.

According to the data obtained, against the background of the development of diastolic dysfunction, tolerance to physical activity is significantly reduced, which is expressed in a decrease in the results of the six-minute walk test (SMT). Patients with diastolic dysfunction have higher scores on the scale for assessing the clinical condition of patients with CHF as modified by V.Yu. Mareeva. In addition, patients with diastolic dysfunction were more likely to suffer from alcohol dependence. The anamnesis of cardiovascular events in patients with diastolic dysfunction is more aggravated by cases of detection of coronary heart disease (CHD), atrial fibrillation, and various specified ventricular arrhythmias. Unsuppressed viral load was more common in the group of patients with diastolic dysfunction. Liver cirrhosis and ascites were more often detected in the group of patients with diastolic dysfunction.

Table 2 presents the main indicators obtained when the author conducted an echocardiographic study of all patients with HIV infection, depending on the presence of diastolic dysfunction. The data obtained indicate significant differences between the groups in the slowdown time of early diastolic filling flow (DFF), LV isovolumic relaxation time (IVRT), and Tei index. Left ventricular hypertrophy (LVH), along with the value of left ventricular myocardial mass index (LVMMI) significantly prevailed in the group of patients with diastolic dysfunction. Left ventricular end-diastolic vo-lume (LV end-diastolic volume) and its ratio to body surface area (BSA) had higher values in the group of patients with diastolic dysfunction. Left atrial volume (LAV) and the number of patients with increased left atrium volume significantly prevailed in the group of patients with identified diastolic dysfunction. The number of patients with pulmonary arterial hypertension and the level of mean pressure in the pulmonary artery significantly prevailed in the group of patients with diastolic dysfunction. High diagnostic compliance for determining diastolic dysfunction was demonstrated by the Tei index and the ratio of the maximum velocity of early filling of the left ventricle to the early diastolic velocity of the annulus fibrosus (E/e') >14.

Table 2

Main indicators characterizing echocardiographic features of diastolic dysfunction in HIV-infected patients

Sign	Diastolic dysfunction present, n=136	Diastolic dysfunction not determined, n=104	p
LVEF, %	55,3 [48,0; 65,0]	55,5 [50,0; 63,0]	0,803
E/A LV	1,18 [0,87; 1,80]	1,3 [1,08; 1,5]	0,180
DT,ms	100,0 [64,0; 120,0]	126,0 [86,5; 181,5]	0,031*
IVRT, ms	68,0 [52,0; 100,0]	88,5 [76,0; 112,0]	<0,001*
Tei Index	0,55 [0,48; 0,70]	0,21 [0,15; 0,33]	<0,001*
LVMI, g/m^2	132,0 [103,0; 177,6]	115,9 [89,0; 131,0]	0,027*
LVH, n (%)	73 (54)	31	<0,001*
LV EDV	97,0 [79,0; 114,0]	88,0 [67,0; 110,0]	0,014*
LV ESR	40,0 [25,5; 54,0]	39,5 [22,0; 51,0]	0,285
OLP index, ml/m^2	36,5 [29,5; 54,0]	27,8 [20,7; 35,4]	0,015*
Increased OLP, n (%)	65 (48)	30 (29)	0,003*
PAH, n (%)	79 (58)	25 (24)	<0,001*
MPAP, mm Hg	29,0 [16,0; 41,3]	16,0 [12,0; 25,0]	<0,001*
EDV LV/PPT	55,83 [45,05; 70,80]	50,0 [40,49; 51,5]	0,046*
ESR LV/PPT	21,67 [16,83; 30,68]	21,3 [14,66; 27,97]	0,431
E/e'	17,3 [13,8; 19,0]	5,8 [4,46; 6,91]	<0,001*

Abbreviations: * – differences in indicators are statistically significant (p <0.05); LVEF% – left ventricular ejection fraction as a percentage; E/A - ratio of the peaks of the maximum speed of early and late filling; DT – flow deceleration time of early diastolic filling; IVRT – LV isovolumic relaxation time; DD – diastolic dysfunction; LVMI – left ventricular myocardial mass index; LVH – left ventricular hypertrophy; LV EDV – end diastolic volume of the left ventricle; LV ESV – left ventricular end-systolic volume; OLP – left atrium volume; PAH – pulmonary arterial hypertension; MPAP – mean pulmonary artery pressure; BSA – body surface area; E/e' – the ratio of the maximum speed of early filling of the left ventricle to the early diastolic speed of movement of the fibrous ring.

The data obtained indicate significant differences between the groups in the slowdown time of early diastolic filling flow (DT), LV isovolumic relaxation time (IVRT), and Tei index. Left ventricular hypertrophy (LVH), along with the value of left ventricular myocardial mass index (LVMI) significantly prevailed in the group of patients with diastolic dysfunction. Left ventricular end-diastolic volume (LV end-diastolic volume) and its ratio to body surface area (BSA) had higher values in the group of patients with diastolic dysfunction. Left atrial volume (LAV) and the number of patients with increased left atrium volume significantly prevailed in the group of patients with identified diastolic dysfunction. The number of patients with pulmonary arterial hypertension and the level of mean pressure in the pulmonary artery significantly prevailed in the group of patients with diastolic dysfunction. High diagnostic compliance for determining diastolic dysfunction was demonstrated by the Tei index and the ratio of the maximum velocity of early filling of the left ventricle to the early diastolic velocity of the annulus fibrosus (E/e') >14. Of course, the disadvantage of this study is the lack of speckle tracking options on hospital ultrasound machines, however, the use of a combination of pulse wave, color and tissue Doppler indicators allows for effective and timely identification of signs of diastolic dysfunction. There are presents the main laboratory changes in HIV-infected patients, depending on the presence of diastolic dysfunction in Table 3.

Table 3

Basic laboratory parameters characterizing the features of diastolic dysfunction in HIV-infected patients

Sign	Diastolic dysfunction present, n=136	No diastolic dysfunction, n=104	p
Serum NT-proBNP, pg/ml	581,2 [261,5; 1474,6]	83,7 [25,2; 206,7]	<0,001*
Cholesterol, mmol/l	3,8 [3,65; 4,55]	3,64 [3,45;5,0]	0,543
Transferrin, mg/dl	92,0 [50,2; 125,7]	113,0 [60,0;161,7]	0,022*
Ferritin, mcg/l	129,25 [61,0; 320,0]	141,0 [73,0; 429,8]	0,460
Serum iron, mcmol/l	2,3 [1,2; 4,7]	2,4 [1,1; 5,9]	0,588
Hemoglobin, g/l	92,0 [74,5; 113,0]	120,0 [99,0; 132,0]	<0,001*
Anemia, n (%)	110 (81)	48 (46)	<0,001*
Severe anemia, n (%)	29 (21)	6 (6)	<0,001*
Mild anemia, n (%)	45 (33)	27 (26)	0,232
Moderate anemia, n (%)	36 (26)	14 (13)	0,013*
Platelets, cells ·10^9/l	164,0 [100,0 ; 261,0]	194,0 [119,0; 269,0]	
Thrombocytopenia,n (%)	60 (44)	39 (37)	0,302
Erythrocytes, cells •10^{12}/l	3,2 [3,0; 3,6]	3,8 [3,3; 4,2]	0,019*
Leukocytes, cells •10^9/l	5,9[4,0; 9,3]	7,3 [6,1; 13,5]	0,056
Lymphocytes, %	16,0 [9,0;23,0]	25,0 [20,0; 30,0]	0,009*
Fibrinogen, g/l	4,0 [3,0; 4,5]	3,5 [3,0; 4,5]	0,361
CD4 T-lymphocytes,	200,0 [41,00; 350,00]	240,0 [76,0; 500]	0,088
Urea	5,7 [4,2; 13,6]	4,7 [3,7; 6,6]	0,011*
NGAL, pg/ml	69,6 [46,1; 267,9]	28,2 [23,0; 130,4]	0,045*
Creatinine, mcmol/l	98,0 [79,0; 148,0]	87,0 [69,0; 105,0]	0,002*
GFR, ml/min/1.73m^2	75,0 [41,0; 97,0]	89,0 [70,0; 113,0]	0,001*
CKD, n (%)	37 (27)	9 (9)	<0,001
ALT, units/l	27,0 [17,0; 60,0]	32,0 [20,5; 55,0]	0,123
AST, units/l	41 [27,0; 86,0]	51,5 [31,5; 79,0]	0,210
Glucose, mmol/l	5,1[4,4; 6,0]	5,0 [4,4; 6,0]	0,691
ESR, mm/h	41,0 [21,0;60,5]	32,0 [15,0; 44,0]	0,007*
Serum CRP, mg/l	23,50 [12,0; 84,0]	28,0 [7,0; 69,0]	0,533
Urine SRP, mg/l	0,8 [0,1; 1,0]	0,0 [0,0; 0,1]	0,027*
Sodium, mmol/l	142,0 [138,0; 144,0]	142,0 [137,0; 146,0]	0,279
Potassium, mmol/l	4,1 [3,6; 4,5]	4,1 [3,8; 4,5]	0,434
Total protein, g/l	68,0 [62,0; 74,5]	69,0 [64,00; 78,00]	0,176
Uric acid, mcmol/l	104,6 [52,8; 207,9]	138,35 [43,2; 163,5]	0,326

Abbreviations: * – differences in indicators are statistically significant (p <0.05); NT-proBNP – N-terminal brain natriuretic propeptide; LDL – low density lipoproteins; CD4 – level of CD4 T-lymphocytes; NGAL, human neutrophil gelatinase-associated lipocalin; GFR – glomerular filtration rate; CKD – chronic kidney disease; ESR – erythrocyte sedimentation rate; CRP – C-reactive protein.

An increase in the concentration of NT-proBNP in diastolic dysfunction is due to manifestations of CHF. There are significant differences between groups of patients associated with the presence of anemia and impaired renal function. Thus, the levels of transferrin and hemoglobin decrease with diastolic dysfunction, which indicates the leading role of anemia in the development of CHF in HIV-infected patients, while the number of patients with severe anemia significantly prevailed in the group with diastolic dysfunction. Glomerular filtration rate in diastolic dysfunction was lower, and serum creatinine and urea concentrations were higher in the group of patients with diastolic dysfunction. The value of human lipocalin associated with neutrophil gelatinase in the group of patients with diastolic dysfunction was almost 3 times higher than the level in patients without diastolic dysfunction. It is known that lipocaine associated with neutrophil gelatinase (lipocaine-2) is a sensitive marker of acute kidney injury and/or an early and very sensitive marker of the development of chronic kidney disease [18]. Serum C-reactive protein (CRP) did not differ significantly between groups, however, the concentration of urinary CRP was significantly higher in the group of patients with diastolic dysfunction, and in patients without diastolic dysfunction in the urine it was practically not detectable. The latter indicates the role of the inflammatory process in the kidneys in the development of diastolic dysfunction. Additionally, the role of inflammation in the formation of diastolic dysfunction is indicated by a significant increase in erythrocyte sedimentation rate. The level of lymphocytes in patients with diastolic dysfunction was significantly lower, which can be explained by the worsening of immunodeficiency in these patients. At the same time, the level of CD4 lymphocytes was reduced in both groups of patients and did not differ significantly. An analysis of the chances and risks for the development of diastolic dysfunction in patients with HIV infection was carried out. The results are presented in Table 4.

Table 4

Results of the analysis of the chances and risks of developing diastolic dysfunction

Index	p	OR and 95%CI	RR and 95%CI
Anemia	<0,001	4,76 (2,67–8,48)	2,14 (1,52–2,98)
Death within 2 years	0,014	3,14 (1,22–8,08)	1,46 (1,15–1,84)
Ventricular arrhythmias	<0,001	3,48 (1,77–6.82)	1,54 (1,26–1,89)
Cardiac ischemia	0,002	3,79 (1,59–9,02)	1,51 (1,24–1,85)
Chronic heart failure	<0,001	13,03 (6,68–25,43)	3,94 (2,47–6,25)
Low transferrin	0,001	4,36 (1,37–13,82)	2,43 (1,02–5,78)
Unsuppressed viral load	<0,001	4,58 (2,5–8,15)	2,10 (1,51–2,93)

When comparing the incidence of diastolic dysfunction depending on the presence of anemia, cytolysis, ventricular arrhythmias, CHF, low transferrin levels and death within 2 years after hospitalization in patients with HIV infection, statistically significant differences were obtained ($p<0.050$). The chances of developing diastolic dysfunction in the presence of anemia increase by 4.76 times (95% CI 2.67–8.48), in the presence of ventricular arrhythmias – by 3.48 times (95% CI 1.77–6.82), with detected ischemic heart disease – 3.79 times (95% CI 1.59–9.02), when detecting a reduced level of transferrin – 4.36 times (95% CI 1.37–13.82). The presence of CHF increases the chances of developing diastolic dysfunction by 13.03 times (95% CI 6.68–25.43). Unsuppressed viral load increases the odds of developing diastolic dysfunction by 4.58 times (95% CI 2.5–8.15). Detected diastolic dysfunction in HIV-infected people increases the chances of developing anemia by 2.14 times (95% CI 1.52–2.98), death within years – by 1.46 times (95% CI 1.15–1.84), ventricular arrhythmias by 1.54 times (95% CI 1.26–1.89), coronary heart disease – by 1.51 times (95% CI 1.24–1.85), CHF – by 3.94 times (95% CI 2.47–6.25), reduced transferrin by 2.43 times (95% CI 1.02–5.78). An inverse relationship was revealed between the development of diastolic dysfunction and taking angiotensin receptor antagonists, so the chances of developing diastolic dysfunction are reduced by 3.45 times when taking sartans (OR = 0.29, 95% CI 0.11–0.75).

Figure 1 shows an ROC curve describing the prognosis of the development of diastolic dysfunction in patients with HIV infection depending on the level of NT-proBNP in the blood plasma. The area under the ROC curve corresponding to the relationship between the prognosis of diastolic dysfunction depending on the level of NT-proBNP in the blood plasma was 0.860±0.024 with a 95% CI of 0.813–0.907. The resulting model turned out to be statistically significant ($p<0.001$). The threshold value of NT-proBNP at the cut-off point was 185.7 pg/ml. If the plasma NT-proBP value is ≥ 185.7 pg/ml, a high risk of developing diastolic dysfunction is predicted. The sensitivity of the method was 80.1%, specificity – 72.5%.

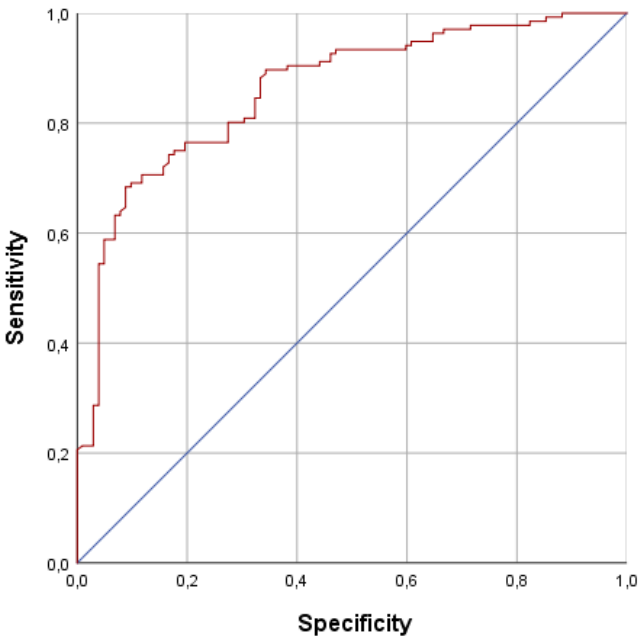

Fig. 1. ROC curve of the relationship between the prognosis of diastolic dysfunction and the value of plasma NT-proBNP in HIV-infected patients

Discussion

Diastolic dysfunction in HIV infection must be diagnosed promptly in order to prevent further worsening of the development of CHF and target organ damage. Against the background of the development of diastolic dysfunction in HIV-infected patients, in our study, tolerance to physical activity significantly decreased, which was evident in a decrease in the results of the six-minute walk test (SWT), symptoms and signs of CHF, noted in the scale for assessing the clinical condition of patients with CHF in modification B, appeared more often .YU. Mareev, which is natural for the development of CHF with preserved EF [1]. Possible alcohol dependence was more often diagnosed in people with diastolic dysfunction, which causes even more intense immunodeficiency in HIV-infected people, aggravates the chronic inflammatory process and oxidative stress; against this background, patients more often refuse antiretroviral therapy and more often suffer from comorbid diseases [9].

Diastolic dysfunction in HIV-infected patients is often asymptomatic, and clinical signs of CHF begin to appear already in the case of the formation of HIV-associated cardiomyopathy with dilatation of the heart cavities, diffuse inflammatory process in the myocardium and diffuse myocardial fibrosis, therefore, in our study, the history of cardiovascular events of patients with diastolic dysfunction is burdened by more frequent cases of detection of chronic coronary heart disease (CHD), atrial fibrillation, and various specified ventricular arrhythmias [1, 10, 11].The inflammatory model of diastolic dysfunction occupies one of the leading places in the pathogenesis of this clinical condition in HIV-infected patients and is based on the fact that many chronic diseases, such as anemia, COPD, chronic kidney disease, diabetes mellitus and others are accompanied by microvascular low-intensity inflammation, which leads to the formation of free radicals and reduces the bioavailability of nitric oxide [15]. Left ventricular hypertrophy (LVH) is a common component of diastolic dysfunction and CHF in HIV-infected patients, as in the work of Okeke NL et al. [11] indicated that LVH is more pronounced in individuals with suppressed immunity and unsuppressed viral load. The risk of developing CHF with preserved ejection fraction is especially high

in HIV-infected people with a viral load of 2,100,000 copies/ml and a CD4 T-lymphocyte level of 200 cells/μl or less, which raises the understanding that immune processes significantly model the risks of developing CHF in HIV-infected people [1]. Our work also revealed the dependence of the development of diastolic dysfunction on the unsuppressed viral load, and also in the group of patients with diastolic dysfunction there were higher values of the left ventricular myocardial mass index and a larger number of patients with its hypertrophy, and the unsuppressed viral load increased the chances of developing diastolic dysfunction by 4.58 times (95% CI 2.5–8.15).Despite the fact that the traditional factors for the development of LVH and increased LVMI, respectively, are male gender, older age and arterial hypertension, HIV infection is the same factor for increased LVMI and the development of LVH [11, 12]. The chances of developing diastolic dysfunction in patients with HIV infection in our study in the presence of ventricular arrhythmias increased by 3.48 times (95% CI 1.77–6.82), with a history of coronary artery disease – by 3.79 times (95% CI 1.59–9.02).

Volume parameters of the left ventricle and left atrium on ultrasound examination had higher values in the group of patients with diastolic dysfunction, which is explained by the development of HIV-associated cardiomyopathy [13].

The number of patients with pulmonary arterial hypertension and the level of mean pressure in the pulmonary artery significantly prevailed in the group of patients with diastolic dysfunction. The literature describes the predominance of pulmonary arterial hypertension in HIV-infected patients in comparison with patients without HIV, associated with the development of CHF [14]. The transformation of diastolic dysfunction into the clinical picture of CHF with the development of shortness of breath, weakness, and fatigue occurs through a weakening of the outflow of blood from the pulmonary veins into the overfilled left atrium with the development of first venous and then mixed pulmonary hypertension [15].

The history of gastrointestinal diseases with diastolic dysfunction is more aggravated by the development of liver cirrhosis and ascites. It is known that fatty liver disease, even in patients without obesity, is accompanied by the development of diastolic dysfunction due to a low-intensity chronic inflammatory process [16]. The prevalence of left ventricular diastolic dysfunction in patients with liver cirrhosis ranges from 25.7% to 81.4% according to various studies and often correlates with the severity of liver failure [17]. Cirrhotic cardiomyopathy, as a complication of liver cirrhosis of any etiology, is often manifested by the development of diastolic dysfunction of the left ventricle with the development of myocardial fibrosis, hypertrophy and subendothelial edema, often accompanied by ascites, and subsequently progresses to systolic dysfunction [18].

In our study, against the background of diastolic dysfunction, the concentration of NT-proBNP in blood plasma increases significantly. The literature describes a close relationship between the concentration of plasma brain natriuretic peptide in HIV-infected patients and the mass of the left ventricular myocardium [12]. Our study revealed a threshold value of NT-proBNP at the cut-off point equal to 185.7 pg/ml; accordingly, with a plasma NT-proBP value ≥185.7 pg/ml, a high risk of developing diastolic dysfunction is predicted. The sensitivity of the method was 80.1%, specificity – 72.5%.

Serum transferrin concentrations and peripheral blood hemoglobin levels were lower in our patients with diastolic dysfunction. There were more patients with anemia, and especially severe anemia with a hemoglobin level ≤70 g/l, in the group with diastolic dysfunction. There is literature data on the secondary development of diastolic dysfunction and its aggravation in individuals with iron deficiency and iron deficiency anemia, and a decrease in the concentration of transferrin, in addition to the formation of iron deficiency, may be due to the intensification of free radical oxidation [17]. The chances of developing diastolic dysfunction in patients with HIV infection in our study in the presence of anemia increased by 4.76 times (95% CI 2.67–8.48), and when a decreased level of transferrin was detected – by 4.36 times (95% CI 1.37–13.82).

Serum creatinine, urea and lipocaine-2 levels in patients with diastolic dysfunction in our study increased significantly, and glomerular filtration rate decreased. The presence of HIV infection in itself is already a risk factor for the development of chronic kidney disease (CKD), occurring against the background of HIV-associated nephropathy, membranous nephropathy against the background of co-infection with hepatitis B and C, membranoproliferative glomerulonephritis, more often associated with contagion with hepatitis C, mixed cryoglobulinemia – all of these diseases, as well as diastolic dysfunction in HIV, are associated with a chronic inflammatory process [19]. Therefore, the erythrocyte sedimentation rate was significantly higher in patients with diastolic dysfunction, and the concentration of C-reactive protein in the urine was also significantly higher.

Patients with diastolic dysfunction were more likely to take angiotensin receptor antagonists (ARA) and proton pump inhibitors. Patients with diastolic dysfunction took significantly more antiretroviral therapy drugs, namely nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors and protease inhibitors. Effective combination antiretroviral therapy is associated with changes in the nature of CHF in HIV from a phenotype with predominantly systolic dysfunction of the left ventricle to diastolic dysfunction [1]. The role of antiretroviral therapy drugs in the development and aggravation of diastolic dysfunction is also described in the literature, especially for the group of protease inhibitors [20].

The formation of diastolic dysfunction in HIV-infected patients is associated with the development of target organ damage that occurs with CHF, as well as other multiple organ pathologies. The results of our study prove that diastolic dysfunction in HIV-infected people increases the risk of developing anemia by 2.14 times (95% CI 1.52–2.98), death within two years by 1.46 times (95% CI 1 .15–1.84), ventricular arrhythmias – 1.54 times (95% CI 1.26–1.89), coronary heart disease – 1.51 times (95% CI 1.24–1.85), CHF – 3.94 times (95% CI 2.47–6.25), reduction in transferrin level – 2.43 times (95%CI 1.02–5.78). An inverse relationship was revealed between the development of diastolic dysfunction and taking sartans, so the chances of developing diastolic dysfunction are reduced by 3.45 times when taking angiotensin receptor antagonists (OR = 0.29, 95% CI 0.11-0.75).

Conclusion

The development of diastolic dysfunction in HIV-infected patients is a factor that provokes the development and progression of CHF, ventricular arrhythmias, coronary heart disease, and anemia. Diastolic dysfunction in HIV-infected people increases the risk of death by 1.46 times within 2 years. An increase in the concentration of NT-proBNP in the blood plasma of patients with HIV infection ≥ 185.7 pg/ml is associated with the development of diastolic dysfunction in them.

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