International Heart and Vascular Disease Journal • Volume 6, № 20, December 2018
Journal of the Cardioprogress Foundation

Left ventricular diastolic function characteristics in patients with chronic heart failure, in relation to the degree of chronic kidney disease, and their dynamics during treatment

U.K. Kamilova*, Z.D. Rasulova, N.A. Nuritdinov, Sh.R. Ibabekova

Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation, Tashkent, Uzbekistan

Authors

Umila K. Kamilova, M.D., Ph.D. doctor of sciences, deputy director of scientific work of Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation, Tashkent, Uzbekistan

Zulfia D. Rasulova, M.D., Ph.D. doctor of sciences, senior researcher of Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation, Tashkent, Uzbekistan

Nutritdin A. Nutritdinov, junior researcher of Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation, Tashkent, Uzbekistan

Shirin R. Ibabekova, M. D. sonographer, junior researcher, Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation, Tashkent, Uzbekistan

Objective. *To study the dynamics of left ventricular diastolic function (LV DF) in patients with I–III functional classes (FC) of chronic heart failure (CHF) during lisinopril and losartan treatment, depending on stage of chronic kidney disease.*

Materials and methods. *We examined 223 patients with coronary artery disease and I–III FC of CHF initially and after 6 months of treatment. The first group (I) contained 118 patients with I–III FC of CHF, who received lisinopril as a standard therapy, whereas the second group (II) received losartan, and included 105 patients with I–III FC of CHF (the average dose of lisinopril was 7.8 ± 2.6, losartan -76.3 ± 25.6 mg/day). All the patients underwent doppler echocardiography, glomerular filtration rate was quantified using MDRD formula (eGFR). Patients were divided into groups according to eGFR levels: 30<cGFR ≤60 mL/min/1.73 m^3 — 67 patients, and 156 patients with eGFR>60 mL/min/1.73 m^3.*

* Corresponding author. Tel. +7–998-979–89-40; +7–998-234–30-77. E-mail: umida_kamilova@mail.ru

Results. *The analysis of initial DF characteristics revealed diastolic dysfunction (DD) in 81.8 % of patients with CHF, and in 59.3 % of cases disturbances like delayed relaxation were prevalent. DF correlated with eGFR. Patients with eGFR≤60 mL/min/1.73 m² had significant reduction (by 6.8 %) of E-wave velocity (p<0.05) compared to patients with eGFR>60 ml/min/1.73 m²; there was a moderate positive correlation between eGFR and E-wave velocity. Patients improved their LV DF characteristics after treatment, with better results for losartan group. Patients of the first and second groups with eGFR≤60 ml/min/1.73 m² had an increase of E-wave velocity by 14.8 % and 15.7 % (p<0.02), respectively; patients with eGFR>60 mL/min/1.73 m² had a trend of E-wave increase by 2.7 % and 7.5 %, respectively, compared to baseline.*

Conclusion. *81.8 % of patients had DD with the prevalence of disturbances of delayed relaxation type. DF correlated with eGFR. Patients with I–III FC of CHF had an improvement of LV DF characteristics with better results for the group of losartan therapy. Patients of both groups with eGFR≤60 ml/min/1.73 m² had a significant increase of E-wave velocity during treatment.*

Keywords: *chronic heart failure, left ventricle diastolic function, renal dysfunction.*

Conflicts of interest: None declared.

Received: 08.08.2018 **Accepted:** 21.08.2018

Chronic heart failure (CHF) is one of the most prevalent, progressive and prognostically adverse cardiovascular disease and is one of the main causes of hospital admissions [1, 2]. The connection between cardiac and kidney pathology have captured scientists' attention a long time ago. The decrease of glomerular filtration rate (GFR) adversely affect the prognosis in patients with chronic heart failure (CHF) [3]. According to a number of authors, structural and morphological changes of left ventricle (LV) myocardium depend on the functional class of CHF and renal dysfunction. High frequency of diastolic dysfunction in patients with chronic kidney disease (CKD) is expected due to left ventricular hypertrophy (LVH), which is seen in half of patients in pre-dialysis with creatinine clearance of 15–35 ml/min according to a number of studies in European, Asian and Latin American nephrology centers [4].

Renal dysfunction (RD) progression is accompanied by the decrease of renal size, changes of left ventricular mass index (LVMI) and increase of eccentric hypertrophy of myocardium. Eccentric hypertrophy was associated with high creatinine level compared with patients with normal blood test values [4, 5]. Even though over the last years it became clear that supportive and kidney function refining therapy can improve prognosis in patients with CHF [5, 6, 7], there is not enough comparative researches on the effect of different groups of medications on heart diastolic function and kidney function in patients with CHF.

The objectives of this study were to investigate the correlation between left ventricular diastolic function (LV DF) and GFR and to estimate the effect of lisinopril and losartan treatment on LV DF, depending on CHF class and RD.

Materials and methods

The study included the examination of 223 patients with coronary artery disease and I–III FC of CHF initially and after 6 months of treatment. The first group (I) contained 118 patients with I FC (28), II FC (51) и III FC (39 patients) of CHF, who received lisinopril as a standard therapy, whereas the second group (II) received losartan, and included 105 patients with c I FC (22), II FC (49) и III FC of CHF (34 patients) of CHF (the average dose of lisinopril was 7.8 ± 2.6, losartan — 76.3 ± 25.6 mg/day). Average age of the patients was 62.3±5.6 years. The therapy included: statins, antiplatelet therapy, bisoprolol, spironolactone 25 mg per day, loop diuretics on demand. All the patients underwent doppler echocardiography with LV DF parameters estimation [8]: peak velocity of early left ventricular filling (E, m/s), peak velocity of late atrial filling (A, m/s), E/A ratio, isovolumetric relaxation time of LV (IVRT, ms), deceleration time of flow velocity during early left ventricular filling (DT, ms) and glomerular filtration rate, which was quantified using MDRD formula (eGFR) [9, 10]. Patients were divided into two groups according to eGFR levels: 30<cGFR ≤60 mL/min/1.73 m³ — 67 patients (29 in the first and 38 in the second group), and 156 patients with eGFR>60 mL/min/1.73 m³ (89 in the first and 67 in the second group).

Statistical analysis of obtained data was done using Microsoft Office Excel 2013, including the use of integral functions such as Statistica 6.0 software. We used a combination of parametric and non-parametric statistic methods with the calculation of the mean values of studied parameters (M), standard deviation (SD), standard error of the mean (m), relative values (frequency %). Statistical significance of the calculations in comparison of the average values was based on Student's test (t) with the calculation of the error probability (p) when checking the normality of distribution (according to the kurtosis criterion). Results were considered statistically significant if p-value was < 0.05. Pearson's test with the calculation of linear correlation coefficient was used for evaluation of correlation between quantitative variables.

Results and discussion

The analysis of initial DF parameters in patients with CHF revealed diastolic dysfunction (DD) in 81.1% of patients with CHF, the decrease of E-wave velocity, increase of A-wave velocity ($p<0.05$), the deviation of E/A ratio and the increase of IVRT time ($p<0.05$) compared with the control group. It is remarkable that the I type (delayed relaxation) of DD was detected in 59.3% (134 patients), the II type (pseudo normal) in 19.5% (44 patients) and III type (restrictive) in 3.1% (7) of patients. The initial parameters of LV DF were comparable in both groups of patients with I–III FC of CHF.

LV DF parameters in patients with I–III FC of CHF are presented in Table 1. E-wave velocity was 0.578±0.093, 0.601±0.136 and 0.684±0.372 m/s in patients with I–III FC of CHF respectively, and was significantly ($p<0.05$) higher (by 15, 5%) in patients with III FC of CHF; IVRT time was 89.38±8.63, 84.6±16.5 and 84.03±14.17 ms respectively and significantly decreased (by 5.7%) in patients with II and III FC of CHF by 5.7% ($p<0.05$) and 6.4% ($p<0.05$) respectively compared with the parameters in patients with I FC of CHF. DT time was 201.5±14.76, 181.1±36.8 and 177.15±42.88 ms in patients with I–III FC of CHF respectively and significantly decreased in patients with II and III FC of CHF by 11.3% ($p<0.001$) and 13.7% ($p<0.001$) respectively compared with patients with I FC of CHF.

The analysis of LV DF disturbances type in dependence of FC of CHF showed that patients with I FC of CHF had DF disturbances in 76% (38 patients) of cases in both groups. At the same time 58% of patients (29) had I type (delayed relaxation) of disturbances and 18% of patients (9) had II type (pseudo normal). Patients with II FC of CHF had DD in 80% (80 patients) of cases in both groups. I type (delayed relaxation) was detected in 60% of cases (60 patients), II type (pseudo normal) in 19% (19 patients) and III type (restrictive) in 2% (2 patients). Patients with III FC of CHF had DD in 81.2% of cases (60 patients) in both groups: I type (delayed relaxation) in 60.3% of cases (44 patients), II type (pseudo normal) in 21.9% (16 patients) and III type (restrictive) in 6.8% (5 patients).

GFR was 50.9±8.8 and 52.7±7.3 mL/min/1.73m^2 in patients of the first and second group with eGFR⩽60 mL/min/1.73 m^2 respectively; and — 79.6±14.8 and 76.96±14.1 mL/min/1.73 m^2 in patients with eGFR⩾60 ml/min/1.73 m^2 respectively. According to eGFR, patients had 1–3 stages of CKD. 54 patients (80.6%) had 3A stage of CKD and 13 (19.4%) patients had 3B stage of CKD among patients with 3 stage of CKD. DF and eGFR parameters had correlation: patients with eGFR ⩽ 60 mL/min/1.73 m^2 had significantly lower (by 6.8%) E-wave velocity ($p<0.05$) comparing with patients with eGFR> 60 mL/min/1.73 m^2. Patients with CHF with eGFR⩽60 and eGFR>60 mL/min/1.73 m^2 had moderate positive correlation between eGFR and E-wave velocity — r = 0.38 and r = 0.46, respectively.

DF parameters had tendency to improvement during lisinopril treatment in the first group of patients with I and III FC of CHF, but still did not reach the necessary reliability value. Patients with II FC of CHF had significant increase of E-wave velocity and E/A ratio by 12.6% ($p <0.005$) and 19.6% ($p <0.001$) respectively

Table 1. **Initial parameters of LV diastolic function in patients with I–III FC of CHF**

Parameter	All patients with c CHF (n=223)			All patients with c CHF (n=223)		
	I FC (n=50)	II FC (n=100)	III FC (n=73)	GFR⩽60mL/min/1.73 m^2 (n=67)	GFR>60mL/min/1.73 m^2 (n=156)	p
E, m\s	0.578±0.093	0.601±0.136	0.684±0.372*	57.8±9.03	61.7±13.4*	p<0.05
A, m\s	0.641±0.140	0.633±0.149	0.624±0.172	62.3±16.3	63.3±15.05	p>0.05
E/A	0.944±0.273	1.01±0.363	1.11±0.455*	0.946±0.385	1.036±0.397	p>0.05
IVRT, ms	89.38±8.63	84.6±16.5*	84.03±14.17*	86.3±12.98	85.04±14.97	p>0.05
DT, ms	201.5±14.76	181.1±36.8**	177.15±42.9**	187.3±37.21	183.0±35.8	p>0.05

* differences are significant ($p<0.05$) comparing with the patients with I FC,
** $p<0.001$

and decrease of A-wave velocity by 10.1% (p<0.02) comparing with baseline.

The II group of patients with I FC of CHF had significant increase of E-wave velocity peak and E/A ratio by 22.7% (p<0.001) and 28.4% (p<0.001), and the decrease of IVRT and DT by 4.6% (p<0.01) and 12.4% (p<0.001) respectively during losartan treatment. Patients with II FC of CHF had a decrease of A-wave velocity by 10.1% (p<0.05), and with III FC of CHF had an increase of E-wave velocity and DT by 12.6% (p<0.01) and 12.7% (p<0.05) respectively comparing with baseline. Improvement of E-wave velocity peak parameters was detected in both groups of patients with eGFR≤60 and eGFR> 60 mL/min/1.73 m^2 during treatment. E-wave velocity increased by 14.8% and 15.7% (p<0.02) in patients from the first and second group with eGFR≤60 mL/min/1.73 m^2 respectively during treatment. Patients with and eGFR> 60 mL/min/1.73 m^2 had tendency to increase of E-wave velocity by 2.7% and 7.5% comparing with baseline.

The results of our investigation of patients with CHF showed that RD can be revealed at the subclinical stage of the disease, when most patients don't have clinical signs of kidney failure. It is believed that RD develops in patients with CHF due to cardiac output decrease, followed by a decrease in arterial bed filling, renal hypoperfusion, increased renal vessels resistance and a decrease of renal blood flow [11]. However, a number of studies have shown that there is no correlation between the parameters of myocardial contractile function and RD in patients with CHF [3]. A number of authors have established that the main type of diastolic dysfunction in elderly and senile patients with diastolic HF is delayed relaxation [12, 13]. At the same time, they identified the features of structural and functional heart disturbances depending on the presence of CKD. It was established that reduced kidney function has an adverse effect on CHF course, which is connected with DF deterioration and, in particular, the increase of isovolumetric relaxation time in patients with I–II FC of CHF.

The positive effect of RAAS blockers can be explained by the reduction of initially high pressure in kidney glomeruli, which can stop the development of glomerulosclerosis [14, 15]. According to the results of some investigations (ORACLE-RF, etc.) ACE inhibitors and ARA have organ-protective and anti-remodeling effects [6]. Positive effects of RAAS blockers became the subject of special discussion after the publication of the LIFE and RENAAL investigations results [10, 14].

Consequently, the estimation of the correlation between the clinical course of the disease and structural and geometric parameters and the functional state of the kidneys is very important for early screening, disease course prognosing and treatment optimization [16].

Kidneys involvement can be considered to be the main factor of CHF progression and, thus, the idea of the kidney function maintenance for secondary prevention in CHF as the main determinant is very reasonable [5, 6, 17].

Conclusion

The analysis of initial DF characteristics revealed DD in 81.8% of patients with CHF, and in 59.3% of cases delayed relaxation type of disturbances were prevalent as well as restrictive type of DD disturbances were prevalent in patients with III FC of CHF. DF correlated with E-wave velocity and eGFR. Patients from the first and the second group with I–III FC of CHF improved their LV DF characteristics after 6-month treatment, with better results for losartan group in patients with I and III FC of CHF. Patients from both groups with eGFR≤60 mL/min/1.73 m^2 had significant reduction of E-wave velocity without statistically significant differences.

Conflict of interest: None declared

References

1. Tereshchenko SN, Zhirov IV, Narusov O. Yu, Mareev YuV., et al. Diagnosis and treatment of chronic and acute heart failure. Clinical recommendations. Cardiological bulletin. 2016;2:23–33. Russian.
2. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2016. European Heart Journal. 2016;37 (27): 2129–2200.
3. Akbari A, Clase CM, Acott P, Battistella M, et al. Canadian Society of Nephrology Commentary on the KDIGO Clinical Practice Guideline for CKD Evaluation and Management. Am J Kidney Dis. 2015;65 (2): 177–205.
4. Shutov AM. Diastolic dysfunction in patients with chronic renal failure. Nephrology and Dialysis. 2002;4 (3): 195–201. Russian
5. Mezhonov EM, Vyalkina Yu.A., Shalaev SV The prevalence of renal dysfunction and its effect on prognosis in patients with acute heart failure. Heart failure. 2017; 18 (2): 87–93. Russian.
6. National recommendations. Cardiovascular risk and chronic kidney disease: strategies for cardio-nephroprotection. Ed. V.S. Moiseeva, N.A. Mukhina. Russian Cardiology Journal. 2014, 8 (112): 7–37. Russian.

7. Levey AS, Inker LA, Coresh J. GFR estimation: from physiology to public health. Am J Kidney Dis. 2014; 63 (5): 820–34.
8. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. European Heart Journal — Cardiovascular Imaging. 2016: doi:10.1093/ehjci/jew082.
9. Mula-Abed WAS, Al Rasadi K, Al-Riyami D. Estimated Glomerular Filtration Rate (eGFR): A Serum Creatinine-Based Test for the Detection of Chronic Kidney Disease and its Impact on Clinical Practice. Oman Med J. 2012;27 (2): 108–113.
10. Stevens LA, Li S, Kurella T, et al. Comparison of the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) Study equations: risk factors for and complications of CKD and mortality in the Kidney Early Evaluation Program (KEEP). Am J Kidney Dis. 2011;57:S9–S16.
11. Damman K, Masson S, Hillege H, et al. Tubular damage and worsening renal function in chronic heart failure. J Am Coll Cardiol Heart Fail. 2013;1:417–24.
12. Solovyov DA. Features of the geometry of the left ventricle in patients with metabolic syndrome and diastolic dysfunction by the type of relaxation disturbance. The young scientist. 2015;20:142–5. Russian.
13. Marinina OS, Efremova OA, Kamyshnikova LA, Logvinenko SI, Pridatchina LS Diastolic dysfunction of the myocardium in patients with chronic heart failure of different genesis. Scientific Result. 2014, 1: 20–3. Russian.
14. Polonsky VM. LIFE: new prospects for losartan. Family medicine. 2016; 6 (68): 70–4. Russian.
15. Arutyunov AG. ACE inhibitors in CHF: the validity of therapy when changing its goals. Difficult patient. 2014, 5: 1–8. Russian
16. Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2014;63 (5): 713–735.
17. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–612.