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CHRONIC KIDNEY DISEASE AND CHRONIC HEART FAILURE: IMPACT ON PROGNOSIS OF THERAPY

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Abstract: Background. Chronic heart failure (CHF) is a serious problem of modern healthcare, being a consumer of significant material resources due to high frequency of hospitalisation and unfavourable prognosis. CHF quite often coexists with a number of comorbidities, among which chronic kidney disease (CKD) is of particular importance

Objective. To evaluate the impact of decreased glomerular filtration rate (GFR) on the prognosis of patients with chronic heart failure (CHF), to analyse clinical practice with regard to the frequency of prescription of pathogenetic therapy for CHF, achievement of target doses depending on the gradation of GFR in patients.

Materials and Methods. Medical data of 102 patients (40 men and 62 women) with CHF of I-IV functional class NYHA were included in the analysis. Inclusion criteria in the register: proven CHF. Chronic kidney disease was assessed by (GFR) calculated by the CKD-EPI formula (ml/min/1.73 m2). The primary endpoint was defined as all-cause death.

Results. (GFR)<60 ml/min/1.73 m2 was registered in 31.2% of patients, more frequently in women (39 and 28.8%, respectively; p<0.001). When dividing patients into phenotypes according to left ventricular ejection fraction (LVEF), no statistically significant differences were found in the distribution of patients according to(GFR). In patients with CHF with low LVEF (HFlEF) and CHF with preserved LVEF (HFpEF), an GFR<45 ml/min/1.73 m2 was associated with an increased risk of endpoints. Analysis of the prescribed pathogenetic therapy showed that in patients with HFlFV the frequency of prescription of angiotensin-converting enzyme inhibitors (ACEIs), β-adrenoblockers and mineralocorticoid receptor antagonists (MCRAs) decreased (p=0.024, 0.007 and 0.01 respectively), while angiotensin receptor and neprilysin inhibitor increased with decreasing(GFR) (p=0.027). In patients with CHFV, a similar trend of decreasing frequency of prescription of IAPPs and MCRAs with decreasing CRP (p<0.001) persisted, but it was compensated by an inversely proportional increase in the frequency of prescription of angiotensin receptor blockers (p<0.001). One hundred per cent of the target dosage was achieved by more than 85% of patients taking AMKR across the entire range of LVEF, whereas for β-adrenoblockers and angiotensin receptor and neprilysin inhibitor/IAPP/angiotensin receptor blockers the percentage of patients receiving the full therapeutic dosage of the drugs was significantly lower. When analysing target doses of pathogenic drugs, the gradations of achieved doses were evenly distributed throughout the entire range of(GFR).

Conclusion. (GFR)<60 ml/min/1.73 m2 occurs in every 3rd patient with CHF in the whole range of LVEF. Decreased(GFR) worsens the prognosis of patients with both CHFlFV and CHFpFV, increasing in direct proportion with the severity of the stage of chronic kidney disease. Inclusion of patients in the surveillance programme within the framework of the CHF service makes it possible to significantly approach the current

treatment to the optimal drug therapy, at the same time, certain efforts are required to overcome the difficulties with titration to target dosages.

Keywords: heart failure, chronic kidney disease, registry, prognosis, treatment.

Introduction. Chronic heart failure (CHF) is a serious problem of modern healthcare, being a consumer of significant material resources due to high frequency of hospitalisation and unfavourable prognosis. CHF quite often coexists with a number of comorbidities, among which chronic kidney disease (CKD) is of particular importance [1]. The concept of cardiorenal syndrome allows explaining these close interrelationships through complex bidirectional and interdependent cardiorenal and renocardial relationships. From a pathophysiological point of view, cardiac and renal diseases share a number of common mechanisms, including inflammatory and immune-mediated, neurohumoral responses, metabolic changes including bone and mineral disturbances, altered haemodynamics and acid-base balance, and the development of anaemia [1]. Taking into account pathogenetic interactions, the presence of CVD increases the probability of CHD and vice versa [2].

The aim of the study was to evaluate the influence of decreased(GFR) on the prognosis of patients with CHF, as well as to analyse the real clinical practice regarding the frequency of prescription of pathogenetic therapy for CHF, achievement of target dosages of drugs depending on the gradation of(GFR) in patients treated in Tashkent regional hospital

Materials and Methods. Medical data of 102 patients with CHF of I-IV functional class according to the New York Heart Association (NYHA) classification, who underwent examination and treatment in Tashkent regional hospital from January 2024 to November 2024, with known CK values were included in the analysis. Inclusion criteria: proven heart failure (HF). Exclusion criteria from the registry: age below 18 years, prisoners, death of the patient, withdrawal from follow-up. All patients included in the study signed a voluntary informed consent for inclusion in the CHF register. Left ventricular (LV) systolic function was assessed according to the recommendations: 1) LV ejection fraction (EF)≥50% corresponds to preserved LV systolic function (CH with preserved LVEF - HFpEF); 2) LVEF≤40% corresponds to reduced systolic function (CH with low LVEF - HFlEF); 3) LVEF 41-49% corresponds to moderately reduced LVEF (HFmrEF) [11]. Diagnostic criteria for arterial hypertension (AH) were in accordance with the recommendations for AH (blood pressure ≥140/90 mmHg) [12]. CKD was assessed by CKD calculated by the CKD-EPI formula (ml/min/1.73 m2) based on plasma creatinine [13]. The following criteria were also taken into account: medication therapy, smoking history, presence of comorbidities: DM, chronic obstructive pulmonary disease, CHD, AH, CHD, angina pectoris, PICS, atrial fibrillation/atrial flutter, ventricular fibrillation/ventricular tachycardia. The primary endpoint was defined as all-cause death. The percentage of drug dosage (<50%, 50-<100%, 100%) was calculated based on the last administration from the target dosage (Table 1).

Statistical analysis of data was performed using Excel 2010 application software package and SPSS Statistics 26.0 statistical software (IBM, USA). Quantitative data having normal distribution were described using arithmetic mean (M) and standard deviations (SD), 95% confidence interval (CI) limits. In the absence of normal distribution, quantitative data were described using median (Me) and lower and upper quartiles (Q1-Q3). Categorical data were described with absolute values and percentages. The following methods of statistical analysis were used: Student's t-test, Pearson's $\chi 2$, Fisher's exact test, post-hoc analysis using Pearson's $\chi 2$ with Benjamini-Hochberg correction, and one-factor analysis of variance (ANOVA). Kaplan-Meier estimates and survival function plots were used to perform survival analyses. Patient survival analyses were also performed using the Cox regression method, which involves predicting the risk of an event occurring for the object in question and assessing the influence of predetermined independent

variables (predictors) on this risk. Risk is treated as a time-dependent function. The basic assumptions underlying the method are that all explanatory variables are independent, linearly affect the event risk, and that the event risks for any two facilities at any time interval are proportional. For all analyses conducted, differences were considered reliable at a two-sided significance level of $p<0.05$.

Results. We included 102 patients (40 men and 62 women), of whom 31.2% had an(GFR)<60 ml/min/1.73 m². The mean age was 67.6±8.76 years, 24.5% of patients were older than 75 years (n=25). The mean body mass index (BMI) was 31.4±6.66 kg/m2, with 50.3% of patients classified as obese (BMI≥30 kg/m2) [14].(GFR)<60 ml/min/1.73 m² was more common in women (39 and 28.8%, respectively; p<0.001). Patients with an GFR<60 ml/min/1.73 m² were more likely to have a history of DM, CHD and atrial fibrillation, as well as being older and showing higher N-terminal fragment of brain natriuretic peptide (NT-proBNP) values with shorter distance in the 6-minute walk test. Data on LVEF were known in 102 patients; when dividing patients into phenotypes according to LVEF, no statistically significant differences were found in the distribution of patients according to(GFR) (Table 3). During the follow-up period 4 endpoints were registered, including 1 (1.2%) case among patients with HFlEF, 2 (1.2%) cases among patients with HFmrEF, and 1 (1.0%) case among patients with HFpEF. In patients with HFlEF and HFpEF, an GFR<45 ml/min/1.73 m2 was associated with an increased risk of the endpoint, increasing with decreasing GFR), while no such pattern was observed in patients with HFmrEF (p=0.890). Analysis of the prescribed pathogenetic therapy showed that in patients with SNNPH the frequency of prescription of angiotensin-converting enzyme inhibitors (ACEIs), β-ABs and mineralocorticoid receptor antagonists (MCRAs) decreased, while angiotensin receptor and neprilysin inhibitors (ARNIs), on the contrary, increased with decreasing(GFR). In patients with HFmrEF, a similar pattern was observed only for MCRAs. In patients with HFpEF, the trend of decreasing frequency of prescription of ACEIs and MCRAs with decreasing GFR remained similar to that of patients with HFlEF, but it was compensated by an inversely proportional increase in the frequency of prescription of angiotensin receptor blockers - ARB. One hundred per cent of the target dosage was achieved by more than 85% of patients taking MCRAs in the whole range of LVEF, whereas for β-ABs and ARNIs/ACEIs /ARBs the percentage of patients receiving the full therapeutic dosage of the drugs was significantly lower. There were no differences in the frequency of reaching the target dosage for β-ABs between the different phenotypes of CHF. For ARNIs/ACEIs /ARBs, the frequency of reaching the 50-<100% and 100% doses was statistically significantly higher among patients with HFpEF than HFmrEF (p=0.005 and 0.027, respectively) and HFlEF (p=0.005 and <0.001, respectively). When analysing target doses of pathogenic drugs, the gradations of achieved doses were evenly distributed throughout the whole range of(GFR) (Fig. 3), thus, no statistically significant differences in achieved doses depending on(GFR) were obtained

Discussion. In the population-based EPOXA-XSN study in 2014, the mean age of patients was 69.9±12.2 years [15]. Although the proportion of elderly patients with CVD increases over time, the mean age of patients in our study was comparable to that in the EPOXA-XSN study, suggesting that age is not a key factor in increasing burden. There is no data on the incidence of CVD in EPOXA-XSN, which can be attributed to the limitations of this study. Due to the existing cardiorenal relationship, the prevalence of CKD in CHF is higher than in the general population. There is limited evidence in the literature of a higher prevalence of CKD in patients with HFpEF compared to those with HFlEF [19]. The prevalence of renal dysfunction, defined as a decreased GRP<60 ml/min/1.73 m², in our study was 34.6% and was not statistically significantly different between patients with SNnFV, SNumFV and SNcFV (p=0.130), and was more common in women (40.2% vs. 26.6%; p<0.001). In the study by I. Löfmanet al. an increase in mortality was observed in patients with CHF with decreasing(GFR) irrespective of age, presence or absence of DM, NYHA class and haemoglobin level:(GFR) 60-89 ml/min/1.73 m² - hazard ratio - OR 0.86 (0.79-0.95),(GFR) 30-59 ml/min/1.73 m² - 1.13 (1.03- 1.24),(GFR) 15-29 ml/min/1.73 m² - 1.85 (1.67-2.07),(GFR)<15 ml/min/1.73 m² - 2.96 (2.53-3.47) compared to(GFR)≥90 ml/min/1.73 m² [20]. According

to our data, the risk of all-cause mortality increased by 2, 2.5 and 4 times at (GFR) 30-44 ml/min/1.73 m², (GFR) 15-29 ml/min/1.73 m² and (GFR)<15 ml/min/1.73 m², respectively; this pattern was characteristic of both patients with HFlEFand HFpEF.

Therapy with blockers of the renin-angiotensin-aldosterone system is standard in CHF, but in real clinical practice, concerns about hyperkalemia or worsening renal function lead to their underuse or suboptimal doses [16]. β-ABs improve the outcomes of patients with HFlEF at all stages of CKD, including patients on dialysis [9]. The use of inSGLT-2 in turn allows not only to improve the prognosis of patients with CHF, but also to slow down the decline in(GFR) [21]. One of the weaknesses of real clinical practice is the use of low doses of drugs, which is associated not only with the problems of patients' adherence to therapy of CHF, but also with low activity of doctors of real clinical practice [22], especially in those cases when stepwise titration of drug doses is required. According to the data of I.V. Fomin et al. out of all patients with CHF taking blockers of renin-angiotensin-aldosterone system and β-αB, only in 30.2 and 19.7%, respectively, the dose of drugs was higher than 50% of the threshold of recommended doses [25]. The proportion of patients taking the target dose did not increase significantly in our study, repeating that in other studies. When dividing patients into subgroups depending on the calculated (GFR), we did not obtain statistically significant differences in achieving target doses of pathogenic drugs in the whole range of LVEF. The frequency of INSGLT-2 prescription among patients with CHF in our study is rather high, but nevertheless there is a potential for further increase, including in the whole range of LVEF, especially in patients with CKD.

Limitations of the study. Limitations of the study include the uneven distribution of patients in the HFlEF, HFmrEF, and HFpEF groups, with a significantly higher number of patients in the SNcPH group, and a small number of patients with GRP<30 ml/min/1.73 m² in the HFlEF and HFmrEF groups.

Conclusion. (GFR)<60 ml/min/1.73 m² occurs in every 3rd patient with CHF in the whole range of LVEF. Decreased(GFR) worsens the prognosis of patients with both HFlEF and HFpEF, increasing in direct proportion with the severity of CHF stage. Inclusion of patients in the observation programme within the framework of the CHF service allows to significantly approximate the current treatment to the optimal drug therapy according to the clinical recommendations for the treatment of CHF, at the same time, certain efforts are required to overcome the difficulties with titration to target doses.

LITERATURE/REFERENCES

1. Schefold JC, Filippatos G, Hasenfuss G, et al. Heart failure and kidney dysfunction: epidemiology, mechanisms and management. Nat Rev Nephrol. 2016;12(10):610-23. DOI:10.1038/nrneph.2016.113
2. Nicolas J, Claessen B, Mehran R. Implications of Kidney Disease in the Cardiac Patient. IntCardiolClin. 2020;9(3):265-78. DOI:10.1016/j.iccl.2020.03.002
3. Ruocco G, Palazzuoli A, terMaaten JM. The role of the kidney in acute and chronic heart failure. Heart Fail Rev. 2020;25(1):107-18. DOI:10.1007/s10741-019-09870-6
4. Beldhuis IE, Lam CSP, Testani JM, et al. Evidence-Based Medical Therapy in Patients With Heart Failure With Reduced Ejection Fraction and Chronic Kidney Disease. Circulation. 2022;145(9):693-712. DOI:10.1161/CIRCULATIONAHA.121.052792
5. Li X, Lindholm B. Cardiovascular Risk Prediction in Chronic Kidney Disease. Am J Nephrol. 2022;53(10):730-9. DOI:10.1159/000528560
6. Pontremoli R, Borghi C, PerroneFilardi P. Renal protection in chronic heart failure: focus on sacubitril/valsartan. Eur Heart J CardiovascPharmacother. 2021;7(5):445-52. DOI:10.1093/ehjcvp/pvab030

7. Wheeler DC, Stefánsson BV, Jongs N, et al. Effects of dapagliflozin on major adverse kidney and cardiovascular events in patients with diabetic and non-diabetic chronic kidney disease: a prespecified analysis from the DAPA-CKD trial. Lancet Diabetes Endocrinol. 2021;9(1):22-31. DOI:10.1016/S2213-8587(20)30369-7
8. The EMPA-KIDNEY Collaborative Group; Herrington WG, Staplin N, et al. Empagliflozin in Patients with Chronic Kidney Disease. New Engl J Med. 2023;388(2):117-27. DOI:10.1056/NEJMoa2204233
9. Banerjee D, Rosano G, Herzog CA. Management of heart failure patient with CKD. Clin J Am SocNephrol. 2021;16(7):1131-9. DOI:10.2215/CJN.14180920
10. Wetmore JB, Yan H, Horne L, et al. Risk of hyperkalemia from reninangiotensin-aldosterone system inhibitors and factors associated with treatment discontinuations in a real-world population. Nephrol Dial Transplant. 2021;36(5):826-39. DOI:10.1093/ndt/gfz263
11. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42(36):3599-726. DOI:10.1093/eurheartj/ehab368
12. Kobalava J.D., Conradi A.O., Nedogoda S.V., et al. Arterial hypertension in adults. Clinical recommendations 2020. Russian Journal of Cardiology. 2020;25(3):3786 [KobalavaZhD, Konradi AO, Nedogoda SV, et al. Arterial hypertension in adults. Clinical guidelines 2020. Russian Journal of Cardiology. 2020;25(3):3786 (in Russian)]. DOI:10.15829/1560-4071-2020-3-3786
13. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604-12. DOI:10.7326/0003-4819-150-9-200905050-00006
14. Dedov I.I., Mokrysheva N.G., Melnichenko G.A., et al. Obesity. Clinical recommendations. ConsiliumMedicum. 2021;23(4):311-25 [Dedov II, Mokrysheva NG, Mel'nichenko GA, et al. Obesity. Clinical guidelines. ConsiliumMedicum. 2021;23(4):311-25 (in Russian)]. DOI:10.26442/20751753.2021.4.200832
15. Fomin I.V. Chronic heart failure in the Russian Federation: what today we know and what we should do. Russian cardiological journal. 2016;(8):7-13 [Fomin IV. Chronic heart failure in Russian Federation: what do we know and what to do. Russian Journal of Cardiology. 2016;(8):7-13 (in Russian)]. DOI:10.15829/1560-4071-2016-8-7-13
16. Khadzegova A.B. Renal function in heart failure - a predictor of the choice of RAAS blockers. RMZ. Medical Review. 2023;7(1):30-5 [Khadzegova AB. Renal function in patients with heart failure - a predictor for selecting RAAS inhibitors. Russian Medical Inquiry. 2023;7(1):30-5 (in Russian)]. DOI:10.32364/2587-6821-2023-7-1-30-35
17. Lawson CA, Zaccardi F, Squire I, et al. Risk Factors for Heart Failure: 20-Year Population-Based Trends by Sex, Socioeconomic Status, and Ethnicity. Circ Heart Fail. 2020;13(2):e006472. DOI:10.1161/CIRCHEARTFAILURE.119.006472
18. Shlyakhto E.V., Belenkov Y.N., Boitsov S.A., et al. Results of interim analysis of the prospective observational multicentre registry study of patients with chronic heart failure in the Russian Federation 'PRIORITY-CHF': baseline characteristics and treatment of the first included patients. Russian Journal of Cardiology. 2023;28(10):5593 [Shlyakhto EV, BelenkovYuN, Boytsov SA, et al. Interim analysis of a prospective observational multicenter registry study of patients with chronic heart failure in the Russian Federation "PRIORITET-CHF": initial characteristics and treatment of the first included patients. Russian Journal of Cardiology. 2023;28(10):5593 (in Russian)]. DOI:10.15829/1560-4071-2023-5593

19. Khan MS, SammanTahhan A, Vaduganathan M, et al. Trends in prevalence of comorbidities in heart failure clinical trials. Eur J Heart Fail. 2020;22(6):1032-42. DOI:10.1002/ejhf.1818

20. Löfman I, Szummer K, Hagerman I, et al. Prevalence and prognostic impact of kidney disease on heart failure patients. Open Heart. 2016;3(1):e000324. DOI:10.1136/openhrt-2015-000324

21. Packer M, Anker SD, Butler J, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. New Engl J Med. 2020;383(15):1413-24. DOI:10.1056/NEJMoa2022190

22. Polyakov D.S., Fomin I.V., Belenkov Y.N., et al. Chronic heart failure in the Russian Federation: what has changed over 20 years of observation? Results of the EPOHA-CHF study. Cardiology. 2021;61(4):4-14 [Polyakov DS, Fomin IV, BelenkovYuN, et al. Chronic heart failure in the Russian Federation: what has changed over 20 years of follow-up? Results of the EPOCH-CHF study. Kardiologiia. 2021;61(4):4-14 (in Russian)]. DOI:10.18087/cardio.2021.4.n1628

23. Greene SJ, Butler J, Albert NM, et al. Medical Therapy for Heart Failure With Reduced Ejection Fraction. J Am CollCardiol. 2018;72(4):351-66. DOI:10.1016/j.jacc.2018.04.070

24. Komajda M, Anker SD, Cowie MR, et al. Physicians' adherence to guideline-recommended medications in heart failure with reduced ejection fraction: data from the QUALIFY global survey. Eur J Heart Fail. 2016;18(5):514-22. DOI:10.1002/ejhf.510

25. Fomin I.V., Polyakov D.S., Vaisberg A.R. 25 years of real clinical practice in the treatment of chronic heart failure in the Russian Federation - are we doing everything right in 2022? Medical Almanac. 2022;4(73):27-37 [Fomin IV, Polyakov DS, Vaisberg AR. 25 years of chronic heart failure treatment in clinical practice in the Russian Federation - are we doing everything right in 2022. MeditsinskiiAlmanakh. 2022;4(73):27-37 (in Russian)].