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DOSE-DEPENDENT EFFICACY AND SAFETY OF DRUGS IN PATIENTS WITH CHRONIC HEART FAILURE?

***Abstract.** Treatment of chronic heart failure (CHF) is very controversial. The question of optimal doses of beta-blockers, ACE inhibitors, aldosterone receptor antagonists, statins in patients with CHF hadn't been definitively resolved. Achieving the maximum tolerated doses of drugs, although associated with reduced mortality, but is accompanied by an increase in side effects of drugs.*

***Keywords:** Chronic heart failure, ACE inhibitors, MRAs, diuretics, statins, treatment.*

The aim. To present and discuss our own clinical and scientific data concerning the role of beta-blockers and inhibitors of the renin-angiotensin aldosterone system, diuretics, statins in the treatment of patients with CHF and optimization of dosage schemes.

Material and methods. The study enrolled 88 patients with CHF of ischemic origin, with sinus rhythm, stage II AB, II-IV FC according to NYHA, 58 – with reduced LV EF (HFrEF) and 30 - with preserved LV EF (HFpEF). The mean age of patients was 69.18 ± 9.97 years, men 52% (n = 46). The median follow-up for patients with CHF was 396 days, the maximum number of follow-up days was 1302 days. During the observation period, 14 endpoints were registered, which accounted for 15.91% of events: deaths 7 cases (8%), strokes 2 cases (2.3%), acute coronary

syndromes 2 cases (2.3%), progressive heart failure 3 cases (3.4%). Survival was assessed by plotting Kaplan-Mayer curves, and the probability of difference between groups was calculated by the criteria of Gehan-Wilcoxon, Cox-Mantel and log-rank test. Risk factors are determined uni- and multi-variant prognostic models are built by regression analysis of proportional hazards of Cox. ROC analysis established the cut-off values of quantitative risk factors.

Results. The increase in the relative risk of adverse cardiovascular events in patients with CHF regardless of LV EF was associated with a daily dose of carvedilol over 25 mg (HR= 1.05; 95% CI 1.009-1.093; p = 0.0171); eplerenone over 12.5 mg (HR= 1.073; 95% CI 1.005-1.144; p = 0.034), torasemide over 5 mg (HR= 1.13; 95% CI 1.021-1.255; p = 0.019); rosuvastatin over 10 mg (HR= 1.107; 95% CI 1.007-1.203; p = 0.035), and the trend in the use of atorvastatin at a dose of less than 10 mg (HR= 1.05; 95% CI 0.951-1.165; p = 0.327) . The use of ramipril in a daily dose of less than 2.5 mg was accompanied by a tendency to reduce by 22% the relative risk of adverse cardiovascular events (HR= 0.78; 95% CI 0.384-1.580; p = 0.491).

Conclusions. Positive treatment outcomes in patients with CHF, regardless of phenotype, were associated with low daily doses of ramipril (<2.5 mg), eplerenone / spironolactone (<12.5 mg), torasemide (<5 mg), rosuvastatin (<10 mg), but with high doses of atorvastatin (> 10 mg).