

Interrelation of Kidney Dysfunctions with Indicators of Clinical-functional State and Remodelling of the Myocardium in Patients with the Chronic Heart Failure

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Original Research Article

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Article History

Received: 18.07.2018

Accepted: 24.07.2018

Published: 30.07.2018

DOI:

10.36348/sjimps.2018.v04i07.023



Abstract: Purpose of the study. To study the relationship between the clinical course, hemodynamic parameters and the functional state of the kidneys in patients with chronic heart failure (CHF). Patients with CHF with progression of the disease have worsened kidney function, clinical course of the disease, accompanied by a decrease in exercise tolerance for SMWT and deterioration in the quality of life, which was most pronounced in patients with renal dysfunction.

Keywords: Chronic heart failure, kidneys, creatinine, glomerular filtration rate, renal dysfunction.

INTRODUCTION

Chronic heart failure (CHF) is one of the most common, progressive and prognostically unfavorable diseases of the cardiovascular system, as well as one of the most frequent causes of hospitalizations [9, 15]. According to epidemiological studies, the prevalence of CHF in Europe and the United States varies from 0,4% to 2%, significantly increases with age, reaching 10% in individuals older than 60 years [8]. In patients with CHF, the presence of renal dysfunction (RD) is a predictor of an unfavorable clinical outcome [7, 11]. The prevalence of RD in CHF varies from 25% to 60% [10]. Reduction of the glomerular filtration rate (GFR) is considered as a marker of unfavorable prognosis in the cardiovascular diseases population, with a GFR<60 ml/min/1,73 m², the mortality risk increases 2,1 times, with a reduced systolic LV function, the risk of death of patients with renal failure (RF) increases by 3,8 times [5, 14, 16].

Purpose of the study

To study the relationship between the clinical course, hemodynamic parameters and the functional state of the kidneys in patients with chronic heart failure (CHF).

MATERIALS AND METHODS

A total of 223 patients with ischemic heart disease (IHD) with I (50), II (100) and III (73) functional class (FC) of CHF were examined. The mean age of patients was 62,3±5,6 years. Patients were divided into 2 groups depending on the estimated eGFR according to the calculated formula obtained in the MDRD (Modification of Diet in Renal Disease Study) [10, 12]: eGFR≤60 ml/min/1,73m² – 67 patients and eGFR≥60 ml/min/1,73m² – 156 patients. The control group consisted of 20 healthy male volunteers, of comparable age. Clinical characteristics of patients are presented in Table-1.

All patients underwent a comprehensive clinical examination, the six-minute walking test (SMWT), the clinical status of the patients assessed on a scale of assessing the clinical state of patients (SACS), assessment of the quality of life (QL) was examined using the Minnesota Living with Heart Failure Questionnaire, echocardiography (EchoCG) [13], dopplerography of the vessels at the level of the common carotid artery (CCA), serum creatinine (Cr) and enzymes in the urine were determined.

Echocardiography (EchoCG) was performed with an assessment of the final diastolic LV size, final systolic LV size, final systolic volume (FSV), final diastolic volume (FDV), ejection fraction (EF). Analysis of diastolic function by definition of parameters: the maximum early filling rate of the left ventricle (E), the maximum late atrial filling rate (A), the E/A ratio, DT is the time of slowing the flow rate into the early filling phase (ms), the isovolumetric relaxation time of the left ventricular (IVRT, ms).

Table-1: Clinical characteristics of patients included in the protocol of a research

Groups of patients	n (%)
Total number of patients	223
Men	139 (62,3%)
Women	84 (37,7%)
CHF I FC	50 (22,4%)
CHF II FC	100 (44,8%)
CHF III FC	73 (32,7%)
Patients with $eGFR \leq 60$ ml/min/1,73m ²	67 (30%)
Patients with $eGFR \geq 60$ ml/min/1,73m ²	156 (70%)
Idiopathic hypertension	210 (94,2)%
Postinfarction cardiosclerosis	83 (37,2%)

The state of nitrogen excretory, ion-controlling and partial (glomerular filtration) of renal functions was assessed by the determination of creatinine (Kr) of blood serum, creatinine clearance, eGFR, enzymes in the urine of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase (ALT, AST, AP), which were determined initially and in the dynamics of treatment in all patients.

Statistical method of data processing. For statistical data processing, the Microsoft Office Excel 2013 software package was used, including the use of the built-in statistical processing functions with the STATISTICA-6.0 program. The methods of variation parametric and nonparametric statistics were used to calculate the mean arithmetic mean of the studied index (M), the standard deviation (SD), the standard error of the mean (m), relative values (frequency,%), the statistical significance of the measurements obtained by comparing the mean values was determined by the criterion Student (t) with calculation of probability of error (p) for checking the normality of the distribution (by the kurtosis criterion) and the equality of general variances (F-Fisher test). For statistically significant changes, a confidence level of $p < 0,05$ was adopted. To study the relationship between quantitative variables, the correlation analysis was used to calculate the Pearson linear correlation coefficient.

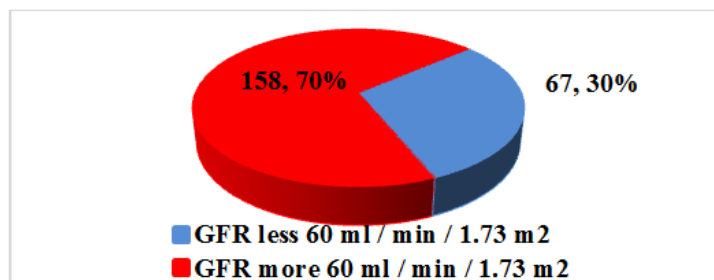
RESULTS

The results of the study showed that in patients with CHF, as the disease progressed, the QL of patients

worsened, with the increase in the clinical manifestations of CHF, a decrease in the exercise tolerance of patients with CHF, which was manifested in a decrease in the SMWT distance, an increase in the SACS score, an increase in the total QL index in both groups.

Evaluation of renal functional status in patients with CHF showed that in 67 (30%) of the patients examined, a decrease in GFR was lower than 60 ml/min/1,73 m² (Fig-1), in 156 patients (70%) GFR more than 60 ml/min/1,73 m², indicating that even "isolated" CHF can lead to impaired renal function.

The association of SMWT and SACS from GFR was proved. Analysis of the parameters of SMWT, SACS and QL in patients with $eGFR \leq 60$ ml/min/1,73 m² showed significant differences between SMWT and SACS in comparison with these parameters in patients with $eGFR > 60$ ml/min/1,73 m². In patients with $eGFR \geq 60$ ml/min/1,73 m² SMWT and the sum of SACS scores were 303,97±89,36 meters and 6,86±2,15 points respectively. In patients with $eGFR > 60$ ml/min/1,73 m²: SMWT and the sum of SACS scores were 350,71±95,55 meters and 5,89±2,26 points (Fig. 2). The SMWT in patients with $eGFR \leq 60$ ml/min/1,73 m² was significantly lower by 14,1% ($p < 0,005$), and SACS by 16% ($p < 0,005$) higher in comparison with these parameters in patients with $eGFR \geq 60$ ml/min/1,73 m².

**Fig-1: Structure of renal dysfunction in patients with CHF**

The high inverse correlations of SMWT with SACS indices ($r=-0,91$ and $r=-0,91$) and SI QL according to the Minnesota questionnaire ($r=-0,88$ and $r=-0,86$) and the mean direct correlation between the

rates of eGFR and SMWT, respectively, in the groups of patients with $eGFR \leq 60$ and $eGFR \geq 60$ ml/min/1,73 m² ($r=0,41$, $r=0,48$).

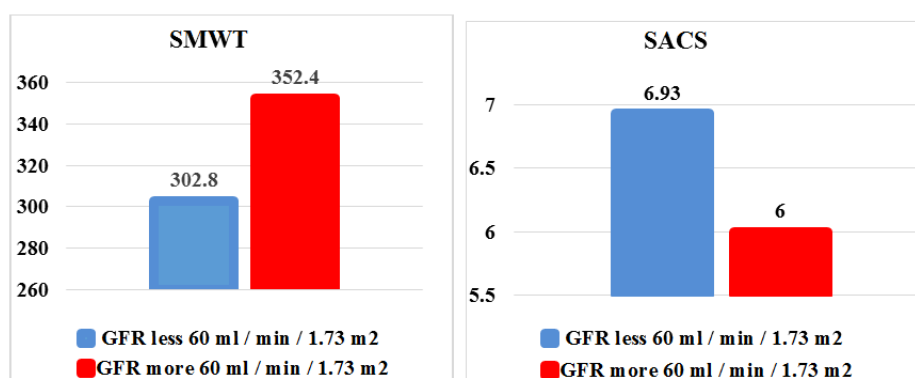


Fig-2: Indicators of SMWT and SACS in patients with GFR less than and more than 60 ml/min/1,73 m²

The results we obtained are confirmed by data from other studies showing a decrease in QL of patients with chronic cardio renal syndrome (CRS) on scales assessing both physical and psychological components of health, with a greater degree of hypochondriac syndrome in patients with chronic cattle, which also negatively affects the quality life and prognosis of patients [2].

The performed analysis of indices of LV remodeling and diastolic function as a function of FC CHF and eGFR showed that the process of pathological cardiac remodeling is accompanied by structural and geometric surgery of the LV with progression of systolic and diastolic dysfunction, which is enhanced when the functional state of the kidneys is impaired, which is confirmed by a series of researches [1].

The relationship between diastolic and systolic function and eGFR was revealed: the early filling rate of LV in patients with $eGFR \leq 60$ ml/min/1,73 m² was 6,7% ($p<0,05$) was significantly lower, LVEF was 8,0% ($p<0,05$), and FSV – by 9,8% ($p<0,05$) higher in comparison with these parameters in patients with $eGFR \geq 60$ ml/min/1,73 m²; ($r=0,38$, $r=0,46$) and between eGFR and LVEF ($r=0,40$, $r=0,38$) in the groups of patients with eGFR and early filling of the left ventricle $eGFR \leq 60$ and $eGFR \geq 60$ ml/min/1,73 m² ($r=0,38$, $r=0,46$).

Disturbances of diastolic function were initially determined in 81,8% (185 patients) of patients of both groups. In this case, type I (delayed relaxation) was recorded in 59,3% (134 patients), type II (pseudonormal) in 19,5% (44), type III (restrictive) in 3,1% (7) patients. Dependence between diastolic and systolic function and eGFR indices was found: the early filling rate of LV in patients with $eGFR \leq 60$ ml/min/1,73 m² by 10,5% ($p<0,05$), LVEF by 8,0% ($p<0,05$) is significantly lower than in patients with

$eGFR \geq 60$ ml/min/1,73 m². In the groups of patients with $eGFR \leq 60$ and $eGFR \geq 60$ ml/min/1,73 m², the mean positive correlation between the eGFR and the rate of early filling of the left ventricle E ($r=0,38$, $r=0,46$) was noted between eGFR and EF LV ($r=0,40$, $r=0,38$). According to a number of studies, the dependence of kidney function on the index – GFR with concentric LVH detected at the earliest stages in patients with chronic kidney disease (CKD) was also determined [1]. The data obtained suggest that even a slight decrease in GFR is a marker of not only progression of CKD, but also myocardial damage [5].

Attention of many researchers attracts the search for new biological markers of tubular lesion in patients with cardio renal syndrome with monitoring of their concentration and characterizing the evolution of renal and cardiac failure [3].

Giperfermenturiya, as a marker, characterizes the dysfunction of glomerular and tubular apparatus in the kidney. In our study, to evaluate the functional state of the kidneys, their tubuloe epithelial system, a method was used to determine the level of enzymes in the urine: ALT, AST and AP. Thus, release of AP is associated with damage to the brush border and the cytoplasmic membrane of the tubular epithelium of the proximal tubules, and the determination of the activity of urinary AP in the urine can be used to assess the degree of damage to surface structures of cytopoiets [1, 4]. The enzymes ALT and AST are in the cytosol of cells, an increase in them indicates a deep damage to the cytoplasmic membranes of the tubular epithelium with the release of the cytosol components into the lumen of the tubules [4].

The results of our study showed a significant increase in the level of enzymes in the urine of ALT, AST and AP in patients with I-III FC of CHF in comparison with the control parameters and an increase

in these indicators as the FC of CHF increases, the level of enzymes in urine can serve as an early marker for assessing the tubuloe epithelial apparatus kidneys, and

can be considered a reliable predictor of renal dysfunction in patients with CHF [4].

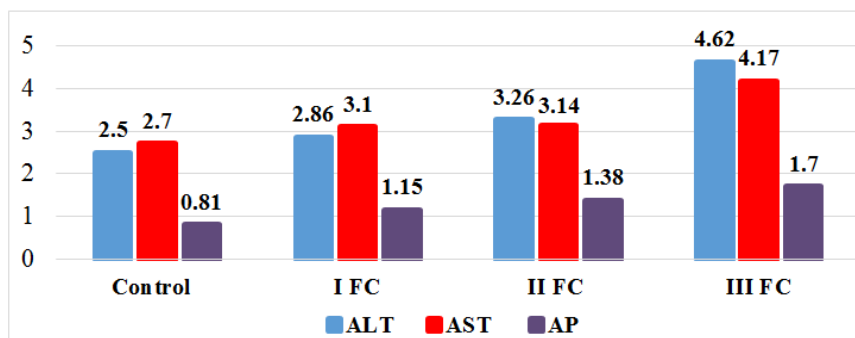


Fig-3: Parameters of the fermenturiya in patients with I - III FC CHF

An analysis of the initial urinary enzyme levels that characterize the functional state of the renal tubules was found in patients with I FC of CHF, the indices of ALT, AST and AP were $2,86 \pm 0,157$; $3,1 \pm 0,138$; $1,158 \pm 0,093$ u/l, which is 11,4% ($p < 0,001$), 13,3% ($p < 0,001$), and 29,7% ($p < 0,001$) higher than those of the control group (Fig. 3). In patients with II FC CHF, ALT, AST and AP were $3,27 \pm 0,222$; $3,15 \pm 0,493$; $1,38 \pm 0,254$ u/l, which is 22,4% ($p < 0,001$), 14,6% ($p < 0,001$) and 40,9% ($p < 0,001$) higher than those of the control group. In patients with III FC, CHF ALT, AST and AP were $4,62 \pm 0,165$; $4,17 \pm 0,191$; $1,7 \pm 0,138$ u/l, which is 45% ($p < 0,001$), 35,6% ($p < 0,001$) and 52,1% ($p < 0,001$) higher than those of the control group.

By determining the level of fermentation and GFR, early detection of subclinical RD in patients with IHD complicated by II-III FC of CHF is possible. Established in our study, a significant increase in the level of enzymes in urine with an increase in the degree of heart failure is an early sign of a lesion of the tubuloe epithelial apparatus of the kidneys, RD in patients with CHF and a predictor of unfavorable prognosis.

CONCLUSION

In patients with CHF with progression of the disease marked significant breach renal function, characterized by reduction $eGFR \leq 60$ ml/min/1,73m², increased levels of enzymes ALT, AST and AP in urine that are predictors of biochemical early RD in patients with CHF. A decrease in $eGFR \leq 60$ ml/min/1,73m² in 30% of patients with CHF were revealed. Giperfermenturiya (rising of level of ALT, AST and AP) as marker, characterizes dysfunction of glomerular and tubular apparatus of kidneys.

Patients with CHF with progression of the disease have worsened kidney function, clinical course of the disease, accompanied by a decrease in exercise tolerance for TSH and deterioration in the quality of life, which was most pronounced in patients with RD. An inverse high correlation with indicators SMWT,

SACS ($r = -0,91$ and $r = -0,91$) and SI QL questionnaire by Minnesota ($r = -0,88$ and $r = -0,86$) and the mean positive correlation between the parameters of eGFR and SMWT, respectively, in the groups of patients with $eGFR \leq 60$ and $eGFR \geq 60$ ml/min/1,73 m² ($r = 0,41$, $r = 0,48$). Patients with $eGFR \leq 60$ ml/min/1,73m² – SMWT index was significantly lower by 14,1% ($p < 0,005$), and SACS above – by 16% ($p < 0,005$) compared to the data rates in patients with $eGFR \geq 60$ ml/min/1,73 m².

In patients with CHF by increasing CHF FC process of pathological cardiac remodeling is accompanied by structural and geometric LV rearrangement with progression of systolic and diastolic dysfunction with a predominance of diastolic dysfunction by type of delayed relaxation in 59% of patients, and in patients with III CHF FC increase in the number of patients with restrictive type of diastolic LV function. A relationship between the indices of diastolic and systolic function and eGFR: LV early filling rate E in patients with $eGFR \leq 60$ ml/min/1,73m² by 6,7% ($p < 0,05$) was significantly lower LVEF - 8,0% ($p < 0,05$), and FSV by 9,8% ($p < 0,05$) higher in comparison with these parameters in patients with $eGFR \geq 60$ ml/min/1,73 m². Marked average positive correlation between eGFR and velocity of left ventricular E early filling ($r = 0,38$, $r = 0,46$) and between eGFR and LVEF ($r = 0,40$, $r = 0,38$) in groups of patients with $eGFR \leq 60$ and $eGFR \geq 60$ ml/min/1,73 m² ($r = 0,38$, $r = 0,46$).

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