NOVATEUR PUBLICATIONS
INTERNATIONAL JOURNAL OF INNOVATIONS IN ENGINEERING RESEARCH AND TECHNOLOGY
[IJIERT] ISSN: 2394-3696 Website: ijiert.org
VOLUME 8, ISSUE 5, May.-2021

# STAGES OF DEVELOPMENT OF RENAL DYSFUNCTION AND ANEMIA IN PATIENTS WITH CHRONIC HEART FAILURE

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## ABSTRACT

Chronic heart failure (CHF) accompanies and is the outcome of most cardiovascular diseases, remaining the same

One of the main reasons for the high level of disability and mortality of patients. Increasing heart failure over time exceeds the danger to the patient's life of the disease that caused heart failure. The prognosis and outcome of CHF is greatly influenced by kidney function. Renal failure is considered as a predictor of survival in patients with left ventricular dysfunction. Currently, the diagnosis of renal dysfunction in patients with CHF is based on the determination of concentration

Serum creatinine, glomerular filtration rate (GFR), and/or the presence of micro albuminuria (MAU) or macro albuminuria.

At the same time, the question of tubular function and the daily profile of renal function (daily filtration rate) in patients with CHF remain insufficiently studied. Anemia associated with CHF continues to attract the attention of researchers. This is the purpose of this work.

**Keywords:** chronic heart failure, kidney disease, anemia, microalbuminuria, N-acetyl –β-D-hexosaminidase.

## INTRODUCTION

115 patients suffering from CHF were examined, including 76 women and 39 men, the average age was 60.4±1.2 years. Distribution of patients according to the etiology of CHF: ischemic heart disease (CHD) + hypertension (GB) - 54 patients (47 %), CHD – 16 patients (14%), GB – 35 patients (30%), rheumatic heart defects outside the activity of rheumatism-10 patients (9%). Patients with kidney disease and / or endocrine pathology were not included in the study. All the subjects were divided into groups depending on the FC of the CHF according to the NYHA classification (1994). The first group consisted of patients with FC I CHF – 48 people, 45 patients had FC II (group 2), 22 patients-FC III-IV (group 3). The control group consisted of 17 practically healthy individuals (average age-60.1 ± 1.3 years). All studies were conducted with the informed written consent of the patients. Renal filtration function was evaluated by GFR using the Cockcroft-Gault formula and creatinine clearance by the Rehberg-Tareev method. The daily filtration rate was determined by calculating GFR according to the latter method 8 times during the day for every 3 hours, and the analysis took into account the average values of creatinine clearance in the daytime and at night. In all patients, the presence of MAU was determined. The activity of N – acetyl – β– D – hexo-zaminidase (NAG) in the morning portion of urine was determined as an indicator of the functional activity of the tubules.

Daily diuresis was taken into account (the average values of minute diuresis in the daytime and at night were calculated), the daily diuresis ratio was calculated. Diuresis/nocturnal diuresis (D/ND), the range of fluctuations in the relative density of urine (OPM) was estimated according to the Zimnitsky sample. The presence of anemia was determined according to generally accepted criteria, using the following indicators: the number of red blood cells, the concentration of hemoglobin, the values of hematocrit (Ht), red blood cell indices (MCV, MCH, MCHC). We evaluated the parameters of iron metabolism – serum iron (CS), total iron-binding capacity of serum (GSS), transferrin iron saturation coefficient (CST).

## RESULTS

The level of serum creatinine in patients with CHF I FC was 85.5±4.2 μmol/l, with II FC-89.9 ± 3.2 μmol/l, III-IV FC – 107.2 ± 8.4 μmol/l, in the control group – 80.2 ± 1.2 μmol / l, while significant differences were found between the indicators of the control group and patients with III-IV FC. When determining GFR, differences were found between the data in the control group and patients with CHF II FC and III-IV FC. The GFR significantly decreased as the FC of CHF increased. In 38% of patients with FC I, GFR exceeded 90 ml / min/1.73 m2, in FC II-in 25% of patients, and normal values of GFR were absent in patients with FC III-IV CHF. Moderate decrease in GFR (60-89. 9 ml / min/1. 73m2) was observed in 38% of patients with FC I, FC II – in39%, and FC III-IV – in 58% of patients. A marked decrease in GFR (30-59. 9 ml / min/1. 73m2) in FC I was found in 19% of cases, in 33% – in FC II, and in 33% – in FC III-IV. In 4% of the examined patients with FC I, 3% – with FC II, and 8% – with FC III-IV, the GFR was less than 30 ml / min/1.73 m2. In patients with FC I, the average CP in the daytime was reduced in 51%, in patients with FC II-in 61%, in 76% of patients with FC III-IV.

All calculated daily mean CP significantly differ from the mean of the control group. The average GFR at night, remaining at the level of normal and subnormal values in patients with FC I, significantly decreases in FC III-IV. The analysis of the daily filtration profile revealed the following. The GFR at night was significantly higher than the GFR during the day and was determined in 72% at FC I, in 73% at FC II, and in 66% at FC III-IV, i.e. in patients with low classes of CHF, the predominance of GFR in the night hours is recorded more often and significantly: in patients with FC I, the average difference between GFR in the night and daytime hours is 21.3%, in patients with FC III-IV-16.0%. Studies of NAG in urine showed its maximum activity in patients with FC I CHF, and as the severity of FC worsened, the activity of the enzyme decreased. Thus, an increase in the level of NAG in the urine was found in 71% of patients with FC I, in 67% of patients with FC II, and in 60% of patients with FC III-IV. NAG values in patients with FC I and FC II CHF significantly exceeded those in the control group. The diurnal rhythm of diuresis, when comparing the average values of D/N, was significantly more disturbed in patients with FC I and II. Thus, DD/ND in patients of this group was 0.89±0.07 (in the control group – 1.2±0.08), in patients with FC II – 0.84±0.04, and in patients with FC III-IV – 0.98±0.06. The range of OPM oscillations was also dependent on the FC of CHF. Less than 7 it was determined in 7% of patients with FC I, in 19% - with FC II, and in 23% - with FC III-IV. In the group of patients with FC I, the hemoglobin concentration was 139.6 ± 2.7 g/l, FC II – 136.2 ± 1.8 g/l, FC III-IV-122.0 ± 6.4 g/l, in the control group –139.4 ± 4.8 g/l. There were significant differences between the parameters in the control group and in patients with III-IV FC. The number of patients with a hemoglobin level of less than 120 g/l increases with the progression of FC CHF: with FC I-0%, with FC II-in 5% of cases (in 3 people out of 45), in 30% of cases (in 3 people out of 10) with FC III-IV. When studying the parameters of iron metabolism (LV, OZHSS, CST) and analyzing the number of red blood cells, Ht values and erythrocyte indices, there were significant differences between patients with CHF in the group as a whole and the control group were not identified. At the same time, there was a decrease in Ht in patients with III-IV FC to 0.35, while in patients with I and II FC it was 0.40. The correlation between the indicators of hemoglobin and the functional state of the kidneys (GFR, MAU, NAG, serum creatinine) was studied. A reliable relationship has not been established.

## DISCUSSION

According to reports, the pathology of the tubules and interstitium is considered a late manifestation of nephropathy in CHF, secondary to the glomerular lesion. In recent years, it has been shown that damage to the tubules and interstitium is not only a manifestation, but also an independent factor in the development and progression of renal failure in many nephropathies. It is known that the determination of the activity of enzymes in the urine can serve as an important criterion for the degree of damage to the tubular apparatus of the kidneys in various pathological processes. Depending on the degree of damage to the urine sequentially enzymes with different intracellular localization are isolated. Thus, with a minor and moderate degree of kidney damage in the urine, the activity of enzymes associated with the brush cell (cytoplasmic and lysosomal) increases. With significant kidney damage, there is an increase in the content of mitochondrial enzymes in the urine, which, as a rule, corresponds to cell necrosis. NAG is a lysosomal enzyme, whose increased activity is characteristic of damage to the proximal tubules. The established maximum activity in

the first FC of CHF may indicate a minor renal injury, and the decrease in the rate of increase of FC of CHF can be considered as an increasing damage to the renal tubular apparatus. Most researchers associate the presence of MAU with a violation of the function of the glomerular filter and an increase in intraglomerular pressure. The increased permeability of the glomerular filter may be due to generalized vascular endothelial dysfunction, changes in the charge of the anionic components of the glomerular basement membrane. The role of proximal albumin reabsorption and albumin degradation during the passage through the tubules requires further study in the genesis of MAU. There is currently no clear answer to the question of which part of the kidney is affected by MAU. The analysis of the obtained data showed that in patients with CHF, against the background of the absence of protein in a single morning portion of urine, determined by conventional methods, there is damage to the glomerular apparatus of the kidneys, as evidenced by the detected MAU. The degree of MAU correlates with the aggravation of FC CHF.

Given the significant increase in the activity of NAG, in comparison with the control group, already in the first FC of CHF, and the detection of MAU only in patients with III-IV FC, it can be assumed that in patients with CHF, the tubular lesion precedes glomerular damage. The degree of decrease in GFR corresponded to the increase in FC CHF: at I – II FC-slightly, at III-IV FC-significantly. Other studies have also shown that glomerular filtration in CHF is maintained at a fairly high level for a long time, significantly decreasing only in patients with severe decompensation of CHF. We found that in CHF, the daily rhythm of the filtration function of the kidneys also changes. A significant (relative to the control group) decrease in GFR during daytime hours was observed in all the examined groups. A significant decrease in GFR at night (in relation to the control group) is determined only in patients with III-IV FC. In addition, in patients with FC I and II, the difference between the mean GFR values in the daytime and at night (in the direction of a relative increase in filtration at night) is recorded at a higher confidence level than in patients with FC III-IV. In other words, patients with I, II FC have a distinct "decomposition" of the daily clearance of endogenous creatinine. The increase in filtration during the night hours is known to be due to improved blood supply the kidneys are at rest and in a horizontal position. There is a certain relationship between the value of GFR and the level of serum creatinine (SC), namely, the increase in SC with a decrease in GFR, but this relationship is not linear. With a moderate decrease in GFR (patients with FC I, II CHF), SC increases unreliably and clearly increases only in patients with FC III-IV. This fact once again confirms the view that GFR, rather than SC, is an indicator of kidney damage, especially in the early stages of CHF. The natural predominance of ND over DD was observed only in patients with I-II FC. Despite the coming oliguria, the average range of OPM fluctuations was within the normal range. At the same time, in patients with III-IV FC, there was an increase in cases with a reduced range of OPM oscillations. The concentration of hemoglobin in patients with CHF significantly decreases as FC worsens: from 139.6 g / l to 122.0 g/l. As FC worsens, the number of patients with a hemoglobin concentration of less than 120 g/l also increases. Ht level is considered to be an independent factor of mortality in CHF. A 1% reduction in Ht increases mortality by 2% over the course of a year. Among patients with CHF, we observed a decrease in Ht at III-IV FC.

## CONCLUSIONS

1) In patients with CHF I-II FC, significant tubular dysfunction was established, as evidenced by an increased content of N-acetyl-β-D-hexosaminidase in the urine, a marker of early damage to the renal tubular apparatus. GFR in patients with FC I does not significantly change, a decrease in the average daily filtration rate is observed in patients with FC II. The diurnal rhythm of GFR is disturbed: a decrease in glomerular filtration in the daytime and an increase in the nighttime hours – the so-called «decomposition» «of the diurnal endogenous creatinine clearance.
2) As the FC of CHF worsens, there is a significant decrease in GFR, microalbuminuria increases, these changes were most significant in patients with FC III-IV. The diurnal filtration curve is marked by a monotonous character: a similar decrease in glomerular filtration in the daytime and at night.
3) The concentration of hemoglobin in the blood and the hematocrit index also decrease with the aggravation of the functional state of patients. No correlation was found between the hemoglobin concentration and the indicators of the functional state of the kidneys.

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