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CENTRAL HEMODYNAMICS IN PATIENTS WITH CARDIORENAL SYNDROME IN DIABETIC NEPHROPATHY

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Abstract
This article presents data on the prevalence of various types of heart remodeling in patients with type 2 diabetes with DN. It was found that the severity of structural and functional changes in the heart depends on the stage of diabetic nephropathy. New data are presented that establish a clear relationship between the indicators characterizing the structural and functional state of the heart and kidneys in patients with type 2 diabetes with DN. New facts have been obtained indicating that the basis of combined renocardial disorders in patients with type 2 diabetes is impaired vascular endothelial function.

Keywords: Diabetes mellitus, diabetic nephropathy, microalbuminuria, glomerular filtration rate, heart remodeling, cardiorenal syndrome.

Relevance:
Diabetes mellitus (DM) is a widespread disease. The number of patients with DM in the world is 140 million people and, according to the World Health Organization, by 2025 this population will increase to 300 million [1,9]. Chronic kidney disease (CKD) is observed in 10-16% of the adult population of Asia, the USA, Australia and Europe and is a global health problem [2,12,14]. It increases the risk of overall mortality and cardiovascular diseases, as well as the possibility

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of progression to terminal renal failure. According to the recommendations of the KDOQI protocols of 2002, CKD is defined as kidney damage assessed by the loss of albumin and a decrease in the glomerular filtration rate (GFR), which underlies its division into stages [3,4,11,16].

The earliest marker of kidney damage in diabetes is microalbuminuria (MAU), the presence of which is closely associated with further progression of diabetic nephropathy [8,10]. With the development of proteinuria, DN progresses to chronic renal failure. 5-10% of DN cases end in terminal stage renal failure, which in the structure of mortality of patients with type 2 diabetes is 1.5-3%. All stages of DN are associated with cardiovascular pathology. The appearance of DN leads to a 5-8-fold increase in mortality in these patients, compared with the general population. Cardiovascular diseases to this day continue to be the leading cause of death in patients with type 2 diabetes who do not survive to the terminal stage of renal failure [5,6,19,20].

Recent studies have described the relationship between GFR and albuminuria and clinical outcome in subjects in the general population, which makes it possible to present threshold values of GFR (<60 ml/min/1.73 m2) and MAU, which are risk factors that increase mortality. Data from epidemiological studies examining more than 65 thousand patients support the viewpoint of MAU as a "biomarker" of adverse outcome even in patients with normal renal function. This allows us to conclude that the concept of MAU should be included in the list of biomarkers indicating both the risk of development and progression of renal dysfunction [6,7,13,20].

Myocardial remodeling in CKD develops due to the influence of a number of factors: pressure and volume overload, anemia, and the effect of a number of pressor hormones [15,17,18]. A number of indicators that determine the degree of renal dysfunction (GFR, creatinine) may play a certain role in hemodynamic impairment and heart failure progression. Based on the above, we studied the relationship between echocardiography indicators of left ventricular (LV) remodeling, the MAU level, and the degree of renal dysfunction in patients with CRS types 2 and 4. The underlying mechanisms that determine the fact of

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combined damage to the heart and kidneys in type 2 diabetes have not been fully studied.

Objective of the Study:
To study the characteristics of cardiorenal syndrome in diabetic nephropathy in patients with type 2 diabetes mellitus.

Material and Methods:
The study included 60 patients (32 men and 28 women) with type 2 diabetes mellitus and DN who were undergoing inpatient treatment at the Republican Scientific and Practical Center of Nephrology based at the III-clinic of TMA. The average age of the patients was 58.0±0.4 years, the duration of type 2 diabetes mellitus was 10.6±0.3 years. The patients (n=60) were divided into 2 groups based on the duration of diabetes mellitus and the level of MAU: in group I (n=25), MAU was within 12.8±4.65μg/ml, in group II (n=35) it was 22.4±4.64μg/ml. The patients underwent general clinical and biochemical tests, B-mode echocardiography.
Echocardiographic examination was performed on the SONOSCAPE S20 ultrasound machine using a 3.5 MHz cardiac sensor in modes according to the generally accepted Simson method.
The glomerular filtration rate (GFR) was determined using the CKD-EPI formula (ml/min/1.73 m2).

Results and Discussion:
In group I patients, the creatinine level and GFR were 76.4 ± 10.8 μmol/l and 79.2 ± 15.8 ml/min/1.73m2, and in group II - 78.2 ± 11.6 μmol/l and 73.4 ± 17.5 ml/min/1.73m2, respectively. Therefore, the higher the MAU level, the higher the creatinine level and the lower the GFR, i.e. initial manifestations of renal dysfunction are noted (Table 1).

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Tab. 1 Characteristics and paraclinical data of patients with CRS

Parameters	Group I	Group II
Age	58.0 ±0.4	58.6± 0.9
BMI (kg/m2)	29.9 ± 4.6*	26.8±3.5*
MAP (мм Hg)	160/100	150/90
Urea (µmol/l)	6.8 ± 1.4	5.6 ± 1.9
Creatinine (µmol/l)	92.3 ± 11.8*	94.2 ± 12.6*
GFR (ml/min/1,73м^2)	74.3 ± 17.5	77.8 ± 16.8

Note. Confidence (*p<0.05)

In patients of group I, DS LV, TPW LV, RWT LV, EF LV and MMILV were observed within the range of 5.18±0.33 cm, 1.16±0.08 cm, 0.47±0.03 M, 9.5±2.9%, 135.9±24.1 g/m2, and in group II - 5.29±0.48 cm, 1.21±0.09 cm, 0.48±0.04, 46.2±4.2%, 156.7±29.1 g/m2, respectively (Table 2).

Table 2 Structural and functional parameters of the myocardium in patients with cattle

Parameters	Group I	Group II
DS LV(N=3.8-5.6 см)	5.18 ± 0.33	5.29 ± 0.48
TIS LV(N=0.7-1.1 см)	1.29 ± 0.11	1.21 ± 0.11*
TPW LV(N=0.8-1.1 см)	1.16 ± 0,08	1.21 ± 0.09
RWT LV(N< 0.45)	0.47 ± 0.03	0.48 ± 0.04
MMI L(г/м^2)	135.9 ± 24.1	156.7 ± 29.1*
EF LV (N- 53% >)	56.2 ± 3.7	46.2 ± 4.2*

Note. Confidence (*p<0.05)

Comparative characteristics of the main structural and functional parameters of the myocardium according to the echocardiography data in patients with chronic CRS reveal that the subjects of group II (MAU-24.8 ± 5.03 µg/ml) have a higher LV DS (5.29 ± 0.48 cm) and a more pronounced decrease in LV EF (52.2 ± 4.2%). The degree of LVH is also significant (LV TPW - 1.21 ± 0.09 cm) in patients of group II (1.16 ± 0.08 cm) than the same indicator in patients of group I (Table 3).

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Correlation analysis revealed a direct proportional relationship between the level of MAU and LV RWT, LV DS and LV MMI, respectively r=0.2, r=0.3, r=0.3 ($p<0.05$) and an inverse relationship between LV EF and MAU (r=(-0.44) moderate correlation $p<0.05$).

Table 3 Kidney function and indicators of LV structural and functional restructuring in patients with cattle

Parameters	Group I	Group II
Age	58.0 ± 0.4	58.6 ± 0.9
MAU (мкg/ml)	14.7 ± 4.45	24.8 ± 5.03*
DS LV (N=3.8-5.6 см)	5.18 ± 0.33*	5.29 ± 0.48*
RWT LV (N< 0.45)	0,47±0,03	0,48±0,04
TPW LV (N=0.8-1.1 см)	1.16 ± 0.08**	1.21 ± 0.09*
TIS LV (N=0.7-1.1 см)	1.26 ± 0.10*	1.31 ± 0.11*
EF LV (N- 53% >)	49.5 ± 2.9**	46.2 ± 4.2**
MMILV(г/м^2)	135.9 ± 24.1	156.7 ± 29.1**
GFR (ml/min/1,73м^2)	89.4 ± 17.3	83.7 ± 19.3
Creatinine (µmol/l)	96.1 ± 18.8	98.3± 17.3

Note. Confidence (*$p<0.05$, **$p<0.01$)

A higher or threshold level of MAU is accompanied by an increase in creatinine and a decrease in SCF, is associated with an increase in LV myocardial mass and is associated with preclinical impairment of LV systolic function.

The interaction of elevated blood pressure, increased LV myocardial mass, changes in its geometry and dysfunction that we identified increases the role of MAU as an early and reliable marker of cardiac, preclinical, structural and functional myocardial changes.

Data from a number of studies indicate the levels of SCF and albuminuria used to define and divide CKD into stages, taking into account complications, the degree of risk and assessment of the effectiveness of managing these patients. Our results allow us to note the level of MAU (22.4 ± 4.64 µg/ml), at which a high probability of impaired LV contractility is determined, which will enable earlier prediction and prevention of CKD progression, and consequently CRS.

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Conclusions

Thus, there are common ethical factors and pathogenetic mechanisms of damage to the heart and kidneys in type 2 diabetes, parallelism in the stages of damage to these target organs. The identified mechanisms of myocardial remodeling in chronic cattle can serve as the basis for early diagnosis of circulatory insufficiency, as well as targeted and pathogenetically justified pharmacotherapy in this category of patients.

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