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ASSESSMENT OF THE CLINICAL AND PATHOGENETIC MECHANISMS UNDERLYING THE PROGRESSION OF CHRONIC KIDNEY DISEASE AND METHODS FOR THEIR CORRECTION

Introduction. Chronic kidney disease (CKD) is a global health priority due to its high prevalence (9-12% of the adult population), relentless progression, and early disability. The progression of CKD to end-stage renal disease (CKD stage 5) involves a complex interplay of hemodynamic, inflammatory, and metabolic factors. Key pathogenetic mechanisms include disturbances in nutritional status (protein-energy wasting, sarcopenia), an imbalance in the matrix metalloproteinase (MMP) system leading to renal fibrosis, and genetically determined features of the renin-angiotensin-aldosterone system (RAAS). Despite current treatment standards, CKD progression rates remain high, highlighting the need for an integrated, personalized approach combining nutritional, molecular, and genetic markers. **Objective:** To study the characteristics of nutritional status and matrix metalloproteinase levels in CKD, evaluate their role in the development of end-stage renal disease, and based on the findings, develop methods for the correction and prevention of disease progression.

Materials and Methods. The study included 576 CKD patients observed in a nephrology hospital from 2021 to 2023. The study design was combined (retrospective and prospective). The retrospective group consisted of 423 patients for clinical course analysis. The prospective group included 153 patients who underwent in-depth examination. Methods included: clinical-anamnestic, anthropometric (BMI, waist circumference), nutritional status assessment using the Subjective Global Assessment (SGA) scale, instrumental methods (Doppler ultrasound of renal arteries with resistance index RI calculation, bioimpedance analysis), laboratory methods (eGFR, proteinuria, ferritin, vitamins B6, D, and folic acid), and molecular-genetic methods (genotyping of AGTR1 A1166C and AGTR2 G1675A polymorphisms, measurement of MMP-2 and MMP-9 levels). Statistical analysis included parametric and non-parametric methods, logistic regression, and ROC analysis.

Results. As CKD progressed, a significant deterioration in nutritional status was observed. The prevalence of nutritional insufficiency (BMI <22 kg/m²)

increased from 6.9% in CKD stage 2 to 33.1% in CKD stage 5 ($p < 0.001$). Multivariate analysis identified high proteinuria (OR=2.64), RI>0.75 (OR=2.25), and anemia (OR=1.62) as the leading independent predictors of rapid progression (eGFR decline >5 mL/min/1.73m²/year). Analysis of RAAS gene polymorphisms revealed no stage-dependent differences; however, carriage of the AGTR1 C/C and AGTR2 A/A genotypes was associated with a trend towards an increased risk of progression (OR>2.0). Serum levels of MMP-2 and MMP-9 significantly increased with CKD severity, showing strong negative correlations with eGFR decline ($r = -0.62$ and -0.58 , respectively). The combined MMP-2+MMP-9 model demonstrated excellent predictive ability for the risk of developing end-stage renal disease (AUC=0.94). Prospective nutritional intervention in the main group ($n=77$) led to significant improvements in body composition (increased skeletal muscle mass, reduced hyperhydration, $p < 0.05$), normalization of vitamin D and folic acid levels ($p < 0.001$), and stabilization of eGFR. Comprehensive intervention (nutritional support + modification of risk factors) reduced the risk of CKD stage progression more than 7-fold (OR=0.13; $p < 0.001$).

Conclusions.

1. Progression of CKD is characterized by a stage-dependent deterioration of nutritional status, transitioning from obesity in early stages to protein-energy wasting and sarcopenia in late stages, necessitating a differentiated correction approach.

2. Polymorphisms of the AGTR1 (A1166C) and AGTR2 (G1675A) genes act as modifying risk factors. They do not determine the disease stage but influence progression rates, with their effects realized primarily at the tissue level in combination with other clinical and metabolic factors.

3. Serum levels of MMP-2 and MMP-9 are highly informative biomarkers for the risk of developing end-stage renal disease, and their combined assessment provides excellent predictive accuracy (AUC=0.94).

4. Stage-oriented personalized nutritional correction is safe, improves the metabolic profile, and optimizes body composition in CKD patients.

5. A comprehensive program integrating nutritional support with the correction of modifiable risk factors significantly slows CKD progression, reduces the risk of transition to end-stage disease, and can be recommended for widespread clinical implementation.

References:

1. Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024;105(Suppl 1):S1-S154.
2. Kalantar-Zadeh K., Fouque D. Nutritional Management of Chronic Kidney Disease. *N Engl J Med.*

2017;377:1765-1776.

3. Fouque D., et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in chronic kidney disease. *Kidney Int.* 2018;73:391-398.
4. Braliou G.G., et al. Renin-angiotensin system gene polymorphisms and chronic kidney disease: a systematic review and meta-analysis. *J Renin Angiotensin Aldosterone Syst.* 2014;15(4):465-478.
5. Heerspink H.J.L., et al. Dapagliflozin in Patients with Chronic Kidney Disease (DAPA-CKD). *N Engl J Med.* 2020;383:1436-1446.
6. Ikizler T.A., et al. KDOQI Clinical Practice Guideline for Nutrition in Chronic Kidney Disease: 2020 Update. *Am J Kidney Dis.* 2020;76(3 Suppl 1):S1-S107.