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LABORATORY CHANGES IN CHRONIC KIDNEY DISEASE CAUSED BY UROLITHIASIS

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Abstract: Based on the analysis of postoperative material from 154 patients with urolithiasis, an assessment of morphological changes in different stages of chronic kidney disease was carried out. It has been shown that morphological changes in chronic kidney disease are characterized by stages and have a correlation with the level of azotemia and glomerular filtration rate. A mathematical model has been developed that allows determining the stage of chronic kidney disease based on morphometric study data.
Keywords: Chronic kidney disease, urolithiasis, morphology

INTRODUCTION: Analysis of literature data showed that most of the works are devoted to the study of CKD in diseases such as glomerulonephritis, diabetes mellitus, hypertension, atherosclerosis, etc., which is even designated in the literature by the term “cardiorenal continuum”. At the same time, there are practically no works devoted to the study of CKD in ICD, while ICD is currently one of the most common urological diseases and accounts for from 0.5 to 5.3% in developed countries. In Russia, ICD accounts for up to 38.2% of all urological patients; most often, this pathology affects people in the most active period of their life - 20-50 years, which undoubtedly represents a huge economic problem of modern healthcare. Currently, CKD is studied from the standpoint of clinical and laboratory diagnostics, while morphological work is practically absent.

MATERIALS AND METHODS: The material for the study was postoperative material obtained from 154 patients who were hospitalized for urolithiasis in the period from 2015 to 2023.

The average age of the patients was 47.1 years. The number of men is 63 (40.1%), women – 91 (59.9%).

The diagnosis of urolithiasis was established on the basis of medical history, subjective and objective clinical signs, ultrasound results, and other instrumental and laboratory research methods.

CKD stage was determined by glomerular filtration rate (GFR) according to the latest NKF-K/DOQI recommendations. GFR was calculated using the Cockcroft-Gault formula, which takes into account the serum creatinine level, age and body weight of the patient.

RESULTS AND DISCUSSION: Based on the results of calculating GFR according to the latest recommendations of NKF-K/DOQI (2005), all patients were divided into 5 groups. As a control, we used sectional material obtained during a forensic medical examination of 30 persons who died from diseases not related to kidney pathology. The age of the control group was 31-52 years (Me=44.0).

Postoperative or biopsy material for histological examination was fixed in 10% neutral formalin, dehydrated in an acetone-xylene battery and embedded in paraffin. After deparaffinization, sections 3-5 μm thick were stained with hematoxylin-eosin for a survey histological examination. To assess the degree of proliferation of connective tissue - picrofuchsin mixture according to the Van Gieson method and trichrome according to Masson, to identify signs of disorganization of the connective tissue, the histochemical method of OKG (orange F, acid red, water blue) was used.

During a standard histological examination, the glomerular apparatus and the condition of the tubulointerstitial zone were assessed using a specific algorithm for studying nephrobiopsy material. To determine the size of objects, we used an eyepiece micrometer, an Avtandilov grid (Avtandilov G.G., 1994), as well as the Bio Vision morphometric system and the automated system for counting morphological changes ARIOL (USA). Morphometric study was performed in 30 fields of vision.

Immunohistochemical study was carried out using monoclonal mouse antibodies to vascular endothelial growth factor, EGFR receptors, to the cytokeratin family: 8, 5/6, 34βE, 10/13. The proliferative activity of renal tubular epithelial cells was studied by immunohistochemical method using

monoclonal mouse antibodies to Ki-67, as well as by detecting the proliferating cell nuclear antigen PCNA. The theory of epithelial-mesenchymal transformation of renal tubular epithelial cells was tested using E-cadherin.

For data processing, the package of applied statistical programs BioStat 5.8.4.3 version 2009 (AnalystSoft® Inc.) and STATISTICA 10.0 (StatSoft® Inc.) was used. Preliminary statistical processing of the data consisted of checking the conformity of the form of distribution of quantitative characteristics to normal, for which the Shapiro-Wilk test was used, as well as the equality of general variances using the Fisher F test. The hypothesis of equality of general means was tested in all cases using the Kruskal-Wallis H test to assess differences between several independent groups. The null hypothesis was rejected if $p < 0.05$. Paired intergroup comparisons were performed using Dunn's Q test. The study of the relationship between quantitative characteristics was carried out using the paired Spearman linear correlation coefficient. The significance of morphometric parameters was determined using discriminant analysis with the measurement of Wilks' lambda level. For each indicator in the studied groups, values such as median (Me), mode (Mo), minimum and maximum values, and interquartile range were calculated.

CONCLUSION: Thus, morphological and morphometric studies of the kidneys showed that structural changes in the kidney have a staged nature of development and quantitative indicators corresponding to a certain stage of development of CKD. A pronounced correlation of varying strength and direction with the glomerular filtration rate and, accordingly, with the stage of CKD and certain morphometric indicators was revealed. It has been established that the morphological signs of kidney damage in the early stages of CKD are: a decrease in the diameter of both distal and proximal convoluted tubules, pronounced thickening of the arterial wall already at the first stage of CKD, and the appearance of focal lymphohistiocytic infiltrates. The second stage of CKD is characterized by the development of compensatory and adaptive processes in the form of hypertrophy of epithelial cells and proliferation of tubular epithelium, confirmed both by conventional staining and by immunohistochemical staining. The proposed mathematical model, based on morphometric indicators, can be used to diagnose the early stages of CKD.

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