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EARLY DIAGNOSIS OF CKD IN COPD PATIENTS

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Annotation. It has now been proven that smoking has an adverse effect on various metabolic processes, causing an increase in the level of free fatty acids, low-density lipoproteins (LDL), glucose and a decrease in the concentration of high-density lipoproteins (HDL), which initiates atherogenesis and, as a consequence, leads to deterioration in renal perfusion [11]. Smoking causes the progression of CKD, inducing glomerular endothelial dysfunction, provoking the occurrence and progression of albuminuria. The results of numerous studies indicate that smoking is a proven risk factor for a decrease in SCF and the development of AU.

Key words: chronic kidney diseases, COPD, diagnosis

In the 25-year MRFIT study (Multiple Risk Factor Intervention Trial), A. Ishani et al . showed that cigarette smoking increases the risk of developing CRF in middle-aged men by 84% compared to non-smokers [5,6]. In the multicenter prospective CRIC study (Chronic Renal Insufficiency Cohort), which included both men and women, showed that smokers and non-smokers with a history of smoking have a higher risk of developing and progressing CKD compared to never smokers [24]. The study by A.S. Ricardo et al, showed that among patients with CKD, non-smokers have a lower risk of developing cardiovascular complications [12]. In the work of D. Chandra et al ., conducted with the participation of 500 smokers, a close statistical relationship was found between the presence and severity of pulmonary emphysema and the degree of decrease in SCF [17]. In a multicenter study, which included more than 600 dialysis patients, it was found that tobacco smoking is a significant risk factor for the progression of CKD [19]. In the works of Y. Bentata et al, it was shown that smoking causes the progression of nephropathy and albuminuria in patients with diabetes [9]. However, as foreign authors show, CKD develops not only in smokers who initially have one or another pathology. Thus, in a recent 6-year prospective study among

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healthy Japanese middle-aged men, an association was found between smoking and a 1.51-fold increase in the risk of developing proteinuria and a 1.32-fold increase in hyperfiltration, as an initial stage of renal dysfunction, due to increased endothelial permeability and increased intraglomerular capillary pressure [7]. The exact mechanism of initiation of renal dysfunction in smokers is still unknown. It has been suggested that cigarette smoke ultimately leads to renal vasodilation and glomerular hyperfiltration mediated by an increase in urinary cyclic guanosine monophosphate and the release of NO and atrial natriuretic peptide [15]. Tobacco smoking provokes oxidative stress, which promotes the catalysis of arachidonic acid peroxidation to 8-isoprostane (8-IP), which leads to an increase in its level. Only in smokers is an inverse relationship found between SCF and 8-IP, which indicates the role of oxidative stress in the formation of the initial stages of renal dysfunction in this category of subjects [5].

Dyslipidemia is associated not only with an increased risk of cardiovascular disease, but is also a risk factor for CKD. The development and progression of renal dysfunction in conditions of hyperlipidemia with the development of glomerulosclerosis and tubulointerstitial fibrosis has been confirmed in a number of animal experiments [9, 15]. Some epidemiological studies have shown that dyslipidemia is associated with a higher risk of developing CKD in the general population [22]. Decreased lipoprotein lipase activity in CKD is an important mechanism for the increase in triglyceride levels, which is observed in these patients [22]. Accumulation of triglycerides and lipid metabolism products in the blood of patients with CKD also has a powerful atherogenic and proinflammatory effect on the cardiovascular system and renal blood flow [23]. Dyslipidemia is common in patients with CKD and is characterized by an increase in plasma triglyceride concentrations, VLDL and a decrease in HDL [13, 21]. Hypercholesterolemia , as is known from many studies, occurs already in the early stages of renal dysfunction and becomes more pronounced with increasing severity of the disease [13, 21].

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There is a large body of evidence linking atherosclerosis and the progression of CKD, leading to increased cardiovascular mortality in patients with CKD. Understanding the pathogenesis of vascular damage in atherosclerosis provides insight into the mechanisms that lead to renal dysfunction. In the walls of blood vessels, circulating lipids are bound and captured by extracellular matrix molecules, where they undergo oxidation [15]. This process is enhanced by elevated plasma lipid levels. Macrophages phagocytose the oxidized lipids, transforming into foam cells that release cytokines, which in turn attract further macrophages, which ultimately impairs endothelial cell function and induces smooth muscle cell migration and proliferation [15]. As a result, smooth muscle cells also accumulate lipids, which disrupts their response to inflammatory stimuli and leads to the accumulation of extracellular matrix, collagen formation; glomerular cells repeat the cascade of these reactions [15]. Thus, such pathogenetic mechanisms contribute not only to the progression of atherosclerosis, but also CKD.

Despite the diversity of morphological forms of CKD, nephrosclerosis develops as a result of each of them. The rate of nephrosclerosis development is determined by both the nature of the disease and the presence of risk factors for CKD progression. In recent years, it has been proven that CKD progression is associated with tubulointerstitial fibrosis in both tubulopathies and glomerulopathies , and a decrease in SCF correlates to a greater extent with the degree of interstitial rather than glomerular lesions [15]. This is primarily due to the fact that the epithelium of the tubular apparatus is more sensitive and, under pathological conditions, is more susceptible to hypoxia than the glomeruli. The overwhelming majority (about 90%) of the intrarenal blood flow is provided by the cortex, which contains most of the glomeruli, thereby ensuring the filtration function. Therefore, even with severe ischemia, the glomeruli can remain undamaged for a long period, unlike the cells of the tubulointerstitium , which undergo atrophy and fibrosis [14]. A vicious circle develops: on the one hand, hypoxia is a consequence of ischemia, on the other hand, it aggravates it. Chronic ischemia, developing as a result of a decrease in glomerular

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blood flow, initially activates the local vasoconstrictor system - RAAS, which causes an increase in intraglomerular pressure with the development of hyperfiltration - an adaptive mechanism for maintaining renal function for some time [11, 14]. Subsequently, under hypoxic conditions, the efficiency of this mechanism decreases, which leads to total glomerular hypoperfusion , as a result of which the SCF decreases and the level of serum creatinine naturally increases . Recent studies show that glomerular hyperfiltration is the initial mechanism for the development of microalbuminuria and kidney damage [18] . Previous activation of RAAS also contributes to the progression of CKD: angiotensin II is a renal growth factor, causing proliferation and phenotypic changes in fibroblasts, which turn into myofibroblasts and increase matrix deposition in the tubulointerstitium [16]. Thus, the following stages are distinguished in the development of nephrosclerosis: glomerular hypertension (hyperfiltration , hypertrophy), tubulointerstitial inflammation and fibrosis [9, 17]. It is noteworthy that CKD is a factor in cardiovascular risk and adverse cardiovascular complications. According to available data, only one third of patients with CKD survive to dialysis, which is due to cardiovascular events [12]. CKD is a well-known predictor of hospitalizations, cardiovascular events and mortality, non-cardiac mortality and all-cause mortality [12, 18]. Decreased renal function is also a risk factor for the development of cognitive dysfunction and decreased quality of life [7].

Thus, in isolated foreign studies of recent years it has been shown that among NCDs not only hypertension and diabetes, but also COPD is associated with the development of renal dysfunction [6, 8]. At the same time, the contribution of systemic manifestations of COPD, as a potential factor in the development and progression of CKD, currently remains poorly understood.

Systemic manifestations of chronic obstructive pulmonary disease as a factor in the development and progression of chronic kidney disease.

COPD is the leading cause of morbidity and mortality worldwide, which is associated with both a high prevalence of up to 20% and pronounced systemic effects of the disease. COPD causes high economic losses - in many countries, its treatment

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accounts for more than half of all funds planned for the treatment of respiratory pathology [5]. The main etiologic factor of COPD is tobacco smoking (active and passive), as well as inhalation of pollutants and combustion products of bioorganic fuels [30]. Throughout the world, especially in countries with high levels of smoking and unfavorable environmental conditions, there is an increase in the prevalence of COPD [18]. Despite the efforts made in the field of health care, including economic costs and the development of preventive programs, statistics indicate a continuing trend towards an increase in mortality due to COPD [3].

Thus, the study of CKD, as the least studied concomitant disease in patients with COPD, is a pressing issue. The development of early diagnostic methods will allow timely nephroprotective therapy and slow down the rate of progression of CKD in this group of patients.

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