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“Yosh olimlar tibbiyot jurnali” O‘zbekiston Respublikasi Oliy ta’lim, fan va innovatsiyalar vazirligi huzuridagi Oliy attestatsiya komissiyasi Rayosatining 2023-yil 5-maydagi 337/6-son qarori bilan tibbiyot fanlari bo‘yicha dissertatsiyalar asosiy ilmiy natijalarini chop etish tavsiya etilgan milliy ilmiy nashrlar ro‘yxatiga kiritilgan.

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Адрес редакции:
Ташкентская медицинская академия 100109, г. Ташкент, Узбекистан, Алмазарский район, ул. Фараби 2,
тел.: +99878-150-7825, факс: +998 78 1507828,
электронная почта: mjys.tma@gmail.com

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ATHEROSCLEROTIC NEPHROPATHY

Nazarova N.O. - Ph.D.
Samig'jonova N.B. - senior teacher
Tashkent Medical Academy. Tashkent, Uzbekistan

Atherosclerosis is considered the major cause of the dramatic increase in cardiovascular mortality among patients suffering from chronic kidney disease (CKD). Although the close connection between atherosclerosis and kidney dysfunction is undeniable, factors enhancing CKD-mediated plaque formation are still not well recognized.

***Key words**: atherosclerosis, chronic kidney disease, plaque.*

АТЕРОСКЛЕРОТИЧЕСКАЯ НЕФРОПАТИЯ

Назарова Н.О. - Ph.D.
Самиғжонова Н.Б. - старший преподаватель
Ташкентская медицинская академия. Ташкент, Узбекистан

Атеросклероз считается основной причиной резкого увеличения сердечно-сосудистой смертности среди пациентов, страдающих хронической болезнью почек (ХБП). Хотя тесная связь между атеросклерозом и дисфункцией почек неоспорима, факторы, усиливающие образование бляшек, опосредованных ХБП, все еще недостаточно изучены.

***Ключевые слова**: атеросклероз, хроническая болезнь почек, бляшка.*

АТЕРОСКЛЕРОТИК НЕФРОПАТИЯ

Назарова Н.О. - Ph.D.
Самиғжонова Н.Б. - катта ўқитувчи
Тошкент тиббиёт академияси. Тошкент, Ўзбекистон

Атеросклероз сурункали буйрак касаллиги (СБК) билан оғриган беморлар орасида юрак-қон томир ўлимининг кескин ўсишининг асосий сабаби ҳисобланади. Атеросклероз ва буйрак дисфункцияси ўртасидаги ўзаро боғлиқликни инкор етиб бўлмайдиган бўлса-да, СБК воситачилигида атеросклероз шаклланишини кучайтирувчи омиллар ҳали ҳам яхши тан олинмаган.

***Калит сўзлар:** атеросклероз, сурункали буйрак касаллиги, пилакча.*

Introduction. The traditional risk factors for cardiovascular morbidity and mortality are not valuable enough when we are talking about chronic kidney disease (CKD) patients. Thus, we can suggest that some supplementary mechanisms and pathogenic processes can participate in emerging CKD-related risk factors [1]. Unfortunately, these specific mechanisms are notsufficiently investigated. On the other hand, very few genes were differentially expressed in healthy arteries from advanced patients with CKD compared to normal renal function individuals. In particular, only 23 genes consistently modulated in vascular smooth muscle cells (VSMCs) were downregulated, and 8 of them were upregulated. Additionally, gene expression was not always accompanied by parallel changes in cellular protein content. For example, both the mRNA expression and the protein content of the alpha subunit of the hypoxia-inducible factor 3 increased as a consequence of uremia, whereas

vimentin content increased with a decreased expression of its mRNA [2].

In patients with CKD, three essential factors of cardiovascular disease (CVD) risk reduction can be noted: (1) accurate diagnosis of CKD, (2) recognition of the elevated risk of CVD, and (3) early identification and modifiable risk factors management [3].

Chronic Kidney Disease (CKD).

The syndrome of a chronicle change in the structure or function of one or both kidneys, which subsequently affects the health, is known as chronic kidney disease (CKD) [4]. Tumors, cysts, malformations, and atrophy, which are noticeable during visualization, are examples of structural abnormalities. Despite this, in children, edema, hypertension, changes in the volume or quality of urine, as well as growth retardation may be signs of alteration of kidney function. Usually, such changes can be detected by increased levels of creatinine, cystatin C, or urea nitrogen in the blood serum. Kidney fibrosis is one of the common pathological manifestations of CKD regardless of the initiating stroke or disease [5].

According to The Kidney Disease Improving Global Outcomes (KDIGO) initiative, if any structure or function violations of the kidneys persist for more than 3 months, the patient can be called a CKD patient [6]. KDIGO presents a severity categorization that describes the different stages of CKD based on glomerular filtration rate (GFR; either estimated (eGFR) or measured (mGFR)) and albuminuria degree. GFR is an established marker of excretory kidney function, and albuminuria, in turn, is an indicator of a violation of the renal barrier (damage to the glomeruli). Both GFR and albuminuria are used to classify CKD and have been declared reliable predictors of long-term chronic kidney disease outcomes [7].

Since the kidney consists of numerous independent functional and anatomical “units” (nephrons), GFR can be expressed by the equation: GFR (total) = GFR (single nephron) the number of nephrons, taking into account that the GFR (single nephron) represents the filtering potential of specific nephrons [8]. This particular equation means that if the number of nephrons is lower, the total GFR does not seem to change as long as the remaining nephrons can elevate their contribution. However, total GFR volume lowering means an essential loss of nephrons, while the remaining nephrons can function at the maximum possible GFR (single nephron) [9].

Thus, CKD represents a loss of the number of nephrons. In addition, the KDIGO categories describe the risk of developing renal failure, e.g., end-stage renal failure (ESRD), which requires renal replacement therapy (peritoneal dialysis, hemodialysis, or kidney transplantation), and several other unfavorable consequences, such as the risk of cardio-vascular disease (CVD), acute kidney injury (AKI), infection, hospitalization, and death. The KDIGO categorization has confirmed its effectiveness in making decisions on patient management, but contradictions still exist [6].

Although the classification of CKD severity by GFR and albuminuria is very valuable, the detection of risk factors for CKD plays an important role in the best management and is recommended by current guidelines [10]. Multiple complications, such as anemia, metabolic acidosis (decreased acid excretion by the kidneys), and cardiovascular diseases, are linked with chronic kidney disease and cause difficulties in patient management [11]. Renal functional reserve (RFR) is the ability of the kidney to enhance the glomerular filtration rate in response to physiological or pathological stimuli or conditions. RFR in clinical practice is determined as the difference between peak ‘stress’ GFR induced by the test and the baseline GFR. When hyperfiltration occurs, RFR may be fully or partially used to achieve normal or supranormal renal function [12]. Classic markers of renal functions (i.e., GFR) can maintain normal ranges up to 50% nephron loss, in contrast to the RFR test, which can represent a sensitive and early way to assess the functional decline in the kidney. Thus, a reduction in RFR may represent the equivalent of renal frailty or susceptibility to insults [13].

More precise prediction of all-cause mortality and fatal/non-fatal CVD was achieved by the calculation of GFR on the base of cystatin C. EGFRcys and albuminuria are independent risk factors for fatal/non-fatal CVD and should be considered in cardiovascular risk prediction to advise primary preventa-

tive treatment decisions [12]. Together with urine albumin–creatinine ratio, which is the marker of albuminuria, eGFRcys was used to create heat maps for the prediction of all-cause mortality, composite fatal/non-fatal cardiovascular disease (CVD), fatal CVD, and end-stage kidney disease. Measuring serum cystatin C is the test that should be used, and eGFRcys can be beneficial for CKD diagnosis and CVD prediction. This can allow the thus making of important clinical decisions around the implementation of CVD risk-lowering therapies in addition to conventional CVD risk factor calculators [11].

Cardiovascular Risk in CKD The main causes of cardiovascular morbidity and mortality do not have the same predictive significance in patients with CKD, especially with progressive CKD, as in the general population [3]. This indicates that additional pathogenic processes are possible, which could be reflected in emerging risk factors associated with CKD.

Cardiovascular Diseases.

The high frequency of cardiovascular diseases in CKD patients may be related to a fairly high prevalence of hypertension, dyslipidemia, hyperuricemia, glucose metabolism disorders, obesity, systemic inflammation, and oxidative stress. People with CKD aged from 25 to 34 years have at least 100 times higher risk of mortality from cardiovascular diseases in contrast to the general population [13].

Cardiovascular changes associated with CKD are similar to the accelerated aging process related to a shortening of telomere length. The underlying mechanisms of accelerated calcification of blood vessels and the heart found in the CCD and ESRD are not sufficiently investigated. In the early stages of CKD (CKD G1–G2), atherosclerotic processes dominate (e.g., invasion of macrophages, plaque formation, and thickening of the arterial wall) [10]. During the development of CKD, inflammatory factors and calcification of media contribute to the degeneration of the vascular wall. The various factors involved cause changes in the profile of risk factors and have different effects on outcomes during CKD. Hypertrophy of the left ventricle is also possible (either concentric (in the case of arterial hypertension) or eccentric (in the case of hypervolemia and anemia)), as well as dilation, which results in systolic and diastolic dysfunction. It was demonstrated that the cause of left ventricular hypertrophy in CKD is early and prolonged induction of fibroblast growth factor 23 (FGF23).

In patients with CKD who have not started renal replacement therapy, the risk of cardiovascular events is as high as in people with diagnosed coronary artery disease. Insulin resistance, high blood pressure, vascular calcification, inflammation, and a decrease in protein-energy levels increase risks. Myocardial stunning is a phenomenon in which transient episodes of ischemia are observed. These episodes can be a result of hemodialysis, which has a direct adverse effect on the heart. Unlike the general population, patients with low GFR or patients on hemodialysis have increased mortality due to adverse cardiovascular events. Thus, CVD risk factors should be intensively managed at all stages.

The determination of atherosclerosis is the main question. Earlier, it was described as a hypothetical atherosclerotic event such as myocardial infarction. This definition has a significant disadvantage since during the sessions of peri-hemodialysis, arrhythmia.

An alternative functional approach may define atherosclerosis as events that can be avoided with the assistance of statin therapy. This definition focuses on clinically significant episodes that indicate a causal relationship as the response to targeted interventions is studied [13]. To determine the effect of atherosclerosis in CKD, randomized clinical trials (RCTs) targeting pro-atherosclerosis factors, in particular, high LDL cholesterol (low-density lipoproteins), are needed [12]. However, this approach has been tested, and the trials keep the same doubts. These doubts are related to the question of whether the failure of such tests indicates different pathogenesis of cardiovascular disease in CKD or the existence of a point-of-no-return. The morphological definition of subclinical atherosclerosis can also be used. It is based on an elevation in the thickness of intima media (IMT), on the presence of plaques during ultrasound examination of the carotid arteries and femur or computed tomography, confirming coronary calcification [14].

Difficulties with this definition include elevated IMT unrelated to atherosclerosis (as reported, for example, for Fabry's disease), coronary calcification unrelated to atherosclerosis, and decreased clinical significance to event-based definitions. A significant amount of imaging data was received due to the evaluation of coronary calcification using computed tomography. Even though these studies imply a higher burden on atherosclerosis in patients with CKD in the general population, autopsy studies report that in developing CKD, calcification sites could be located in the media layer, which is not typical for atherosclerosis in the general population. These autopsy reports coincide with the widespread use of calcium-based phosphate binders and high doses of calcitriol. It is necessary to conduct large population studies comparing CKD with patients who do not suffer from CKD to assess the relative prevalence of atherosclerosis in CKD using morphological determination. The advantage of this definition is that for clinical trials of measures aimed at combating atherosclerosis, it is possible to select patients who have already developed atherosclerosis, while the current approach assumes the appointment of measures aimed at combating atherosclerosis based on risk indicators for the population. The current approach could result in the appointment of measures aimed at the therapy of atherosclerosis to those patients who do not suffer from this disease. Therefore, the result of this intervention will not benefit. At the level of clinical trials, modern approaches may hinder the ability to quantify the actual benefits of drugs that persistently lead to manifestations of atherosclerosis in people suffering from this inflammatory disease. Since the major problem of atherosclerosis associated with CKD is the insufficiency of RCTs with positive results, it was decided to focus on atherosclerosis, which is defined as the presence of plaques as a potential approach to eliminating existing limitation.

Pathogenesis of Atherosclerosis.

Under normal conditions, endothelial cells of the arterial wall resist leukocyte adhesion and aggregation. When the endothelium is damaged due to cigarette smoking or hypertension, LDL molecules infiltrate the arterial wall and are oxidized by intima enzymes. The consequences of this process are activation of endothelial cells and elevated regulation of several types of leukocyte adhesion molecules [14]. These molecules give leukocytes along the vascular surface the opportunity to adhere to the activation site. It was revealed that the vascular cell adhesion molecule-1 (VCAM-1) is of key importance in this process. Monocytes and lymphocytes most often bind to VCAM.

After fixation, chemokines produced in the underlying intima promote the migration of these cells through the intraendothelial junctions and into the subendothelial space. Nowadays, the chemoattractant cytokine monocyte chemoattractant protein-1 is recognized as a key factor that favors the migration of monocytes. It interacts with the C-C chemokine receptor type 2

Conclusions.

It was shown that in the general population with preserved kidney function, cardiovascular diseases are best prevented by minimizing the risk of atherosclerosis. In end-stage renal failure and chronic kidney disease, the atherosclerotic plaque turns out to be a smaller element of the overall burden of CVD. The main components of cardiovascular diseases in patients with CKD are extensive calcification of blood vessels and plaques, as well as endothelial dysfunction. This has a curious and unusual connection with the uremic environment since transplantation lowers the observed MACE compared to patients on hemodialysis or peritoneal dialysis. The approach to this type of atherosclerotic cardiovascular disease was complex, and the currently available treatment methods have not resulted in a significant decrease in ASCVD in individuals with chronic kidney disease, except statins in patients with CKD before dialysis. Nowadays, the presented data force us to raise questions about the expediency of revascularization of coronary arteries in people with CKD and CAD.

References.

1.Pálsson, R.; Patel, U.D. Cardiovascular Complications of Diabetic Kidney Disease. Adv. Chronic Kidney Dis.2014,21, 273–280.

2.Chu, C.P.; Liu, S.; Song, W.; Xu, E.Y.; Nabity, M.B. Small RNA sequencing evaluation of renal microRNA biomarkers in dogs withX-linked hereditary nephropathy. Sci. Rep. 2021,11, 17437.

3.Vallianou, N.G.; Mitesh, S.; Gkogkou, A.; Geladari, E. Chronic Kidney Disease and Cardiovascular Disease: Is there Any Relationship? Curr. Cardiol. Rev. 2019,15, 55–63.

4.Vaidya, S.R.; Aeddula, N.R. Chronic Renal Failure. [Updated 2021 Jul 16]. In StatPearls [Internet]; StatPearls Publishing: Treasure Island, FL, USA, 2021.

5.Menn-Josephy, H.; Lee, C.S.; Nolin, A.; Christov, M.; Rybin, D.V.; Weinberg, J.M.; Henderson, J.; Bonegio, R.; Havasi, A. Renal Interstitial Fibrosis: An Imperfect Predictor of Kidney Disease Progression in Some Patient Cohorts. 2016,44,289–299.

6.Ketteler, M.; Block, G.A.; Evenepoel, P.; Fukagawa, M.; Herzog, C.A.; McCann, L.; Moe, S.M.; Shroff, R.; Tonelli, M.A.;Toussaint, N.D.;et al. Executive summary of the 2017 KDIGO Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD)

7. Khwaja, A. KDIGO Clinical Practice Guidelines for Acute Kidney Injury. Nephron Clin Pract. 2012,120, c179–c184.

8.Romagnani, P.; Remuzzi, G.; Glassock, R.; Levin, A.; Jager, K.J.; Tonelli, M.; Massy, Z.; Wanner, C.; Anders, H.-J. Chronic kidney disease. Nat. Rev. Dis. Primers 2017, 3, 17088.

9.Bianchi, S.; Aucella, F.; De Nicola, L.; Genovesi, S.; Paoletti, E.; Regolisti, G. Management of hyperkalemia in patients with kidney disease: A position paper endorsed by the Italian Society of Nephrology. J. Nephrol. 2019, 32, 499–516.

10. Levin, A.S.; Bilous, R.W.; Coresh, J. Chapter 1: Definition and classification of CKD. Kidney Int. Suppl. 2013,3, 19–62.

11.De Moor, B.; Vanwalleghem, J.F.; Swennen, Q.; Stas, K.J.; I Meijers, B.K. Haemodynamic or metabolic stimulation tests to revealthe renal functional response: Requiem or revival? Clin. Kidney J. 2018,11, 623–654.

12.Lees, J.S.; Welsh, C.; Celis-Morales, C.A.; Mackay, D.; Lewsey, J.; Gray, S.R.; Lyall, D.M.; Cleland, J.G.; Gill, J.M.R.; Jhund, P.S.; et al. Glomerular filtration rate by differing measures, albuminuria and prediction of cardiovascular disease, mortality and end-stage kidney disease. Nat. Med. 2019,25, 1753–1760.

13.Chazot, R.; Botelho-Nevers, E.; Mariat, C.; Frésard, A.; Cavalier, E.; Lucht, F.; Delanaye, P.; Maillard, N.; Gagneux-Brunon, A.Cystatin C and Urine Albumin to Creatinine Ratio Predict 5-Year Mortality and Cardiovascular Events in People Living With HIV.J. Infect. Dis. 2021,223, 885–892.

14.Mihai, S.; Codrici, E.; Popescu, I.D.; Enciu, A.-M.; Albulescu, L.; Necula, L.G.; Mambet, C.; Anton, G.; Tanase, C. Inflammation-Related Mechanisms in Chronic Kidney Disease Prediction, Progression, and Outcome. J. Immunol. Res.2018,2018, 2180373.